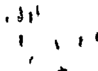
CLINICAL APPLICATIONS OF CARDIOPULMONARY PHYSIOLOGY

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PAUL B HOEBER, INC
MEDICAL DIVISION OF HARPER & BROTHERS

CLINICAL APPLICATIONS OF CARDIOPULMONARY PHYSIOLOGY

Printed in the United States of America

Published October 1960

For information address Paul B Hoeber Inc
Medical Division of Harper & Brothers
49 East 33rd Street New York 16 N Y

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Library of Congress catalog card number 60-15967

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PREFACE

Developed originally as research tools, techniques for the study of cardiorespiratory function have proved valuable in the diagnosis and assessment of many patients with diseases of the heart and lungs Yet both techniques and theory have developed so rapidly in the past ten years that often the physician is forced to rely on others for interpretation of the results of the various studies performed on his patients

It is the intent of this book to outline normal cardiopulmonary physiology, to point out the areas that may be assessed by physiological techniques and to indicate the bearing that such studies have on the diagnosis evaluation and treatment of patients with cardiopulmonary disease Disease of the heart and lungs has been considered as a unit for many reasons Disorder of the heart is frequently manifested by symptoms attributable to the lungs dyspnea for example, while a serious complication of many forms of pulmonary disease is right ventricular failure The functioning of the two organs is intimately interwoven and a primary task of each the supply of oxygen to the tissues is the same This synthesis of function is indicated by the establishment of cardiorespiratory laboratories for the study of patients and most physicians have these laboratory facilities available to them It is hoped that the information presented in this book will be of value to the physician in helping him select the studies indicated for the proper evaluation of his patients In addition an understanding of normal and abnormal cardiopulmonary physiology will provide both student and practitioner with a basis for the evaluation of clinical signs and symptoms which may occasionally serve as a substitute for more precise measurements of disturbed function

This is not a detailed textbook of techniques of cardiopulmonary disease or a review of the literature Rather it is a distillation of personal experience and is designed to present an approach to clinical

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to key articles and books which substantiate and an points developed in the text When one reference suffice not been included No attempt has been made to compile encyclopedia of the voluminous literature in this rapidly

It is impossible to acknowledge the help of all of th have made direct or indirect contributions to this bo whom I am particularly indebted are Dr Herman Tarr continuously helpful advice and encouragement Dr Frank Dr Bruce Sobol, Dr Samuel Fox, Dr Charles and Mrs Eunice C Stevens, for their careful reviews script, and Dr Lenore R Zohman, for assistance in t patients at Grasslands Hospital Finally, I am indebted t Waine for the original illustrations

New York

CHAPTER 1

NORMAL CARDIOPULMONARY PHYSIOLOGY

The physiology of respiration and circulation is depicted schematically in Figure 1 In essence the cardiorespiratory system consists of two pumps a lung pump which intermittently pumps air in and out of the alveoli and a double heart pump which pumps blood through two capillary networks in one continuous circle Actually the heart is located in the center of the chest, the lung pump and is subject to the same pressure changes that cause air to flow in and out of the lungs

The primary function of this entire system is to provide adequate quantities of oxygen to the cells and to remove carbon dioxide The ultimate source of oxygen is the atmospheric air which is also the depository for carbon dioxide

The heart consists of two pumps the right and left ventricles The right ventricle pumps blood from the right atrium to the lungs There oxygen diffuses into the blood from the alveoli and carbon dioxide diffuses out of the blood into the alveoli The lung pumps fresh air in and out of the alveoli so that the alveolar gas composition remains relatively constant in the face of this continuous oxygen uptake and carbon dioxide production Blood flowing from the lung into the left atrium is pumped forward by the left ventricle to the tissues in which oxygen is extracted and carbon dioxide is added The venous blood then flows to the right atrium, whence it is once again pumped to the lung

The final factor in the exchange of gases between the atmospheric air and the tissues is the chemical composition of the blood The hemoglobin contained in the red blood cells has a great affinity for

MEAN PRESSURE FLOW AND THE VOLUME OF BLOOD IN THE CIRCULATORY SYSTEM

The rate at which blood flows through the circulatory system depends upon the arterial pressure and upon the resistance to blood flow offered by the blood vessels The immediate source of the arterial pressure the pumping action of the ventricle will be considered later In this section attention will be directed to the relationships that exist between pressure and blood flow in the vessels

STATIC SYSTEM

In order to understand the factors that affect the magnitude of the pressure in the various portions of the circulatory system it is helpful to examine the responsible factors in a simplified static system In such a system the pressure is the same throughout Its magnitude depends upon two factors the volume of blood in the system and the compliance of the vessel walls The magnitude of the pressure is directly proportional to the amount of blood in the system the more blood the higher the pressure It is inversely proportional to the compliance of the vessel walls the more compliant the walls the lower the pressure

In the human circulatory system the various vessels have different degrees of compliance The veins are very compliant, whereas the arteries are relatively rigid As a result more blood is contained in the veins than in the arteries In the absence of blood flow the pressure is the same in the arteries and veins but the distensible veins hold much more blood than do the arteries

FLOWING SYSTEM

Effect of Cardiac Action

The pressure in any vessel is immediately dependent upon the amount of blood in that vessel and upon the compliance of the vessel wall When blood flows through the system additional pressure is generated by the action of the ventricles Cardiac action has a direct effect on the pressure within the system primarily upon the arterial pressure and indirect effects upon the pressure in other vessels such as the veins

oxygen, that is, large volumes of oxygen are transported to the tissues in a relatively small volume of blood In addition, the oxygen dissociation curve of hemoglobin is such that the hemoglobin is almost fully saturated with oxygen at the partial pressure of oxygen existing in the

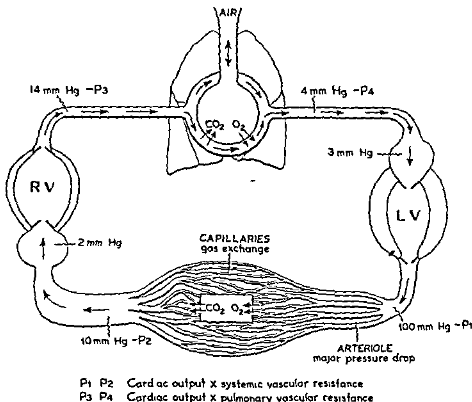


Fig 1 Schematic drawing of normal cardiospiratory system Arterial blood flows through the tissues where oxygen is released and carbon dioxide is taken up Venous blood is pumped to the alveoli where carbon dioxide is given off and oxygen is taken up The lung pumps air into and out of the alveoli to maintain a constant alveolar gas composition in the face of this continuous gas exchange The mean pressure in the systemic arterial system (P1) is much higher than that in the pulmonary artery (P3) because the systemic vascular resistance is much greater than the pulmonary vascular resistance Also the pressure drop across the systemic arterioles (P1 — P2) is correspondingly greater than that across the pulmonary arterioles (P3 — P4) even though the amount of blood flowing through the two beds is the same

alveoli whereas it gives up a large amount of oxygen to the tissues when exposed to the lower oxygen tension existing in and around the cells This aspect of cardiopulmonary physiology will not be considered here but the action of the heart and lung pumps will be discussed in some detail

to causing an increase of arterial pressure, arteriolar constriction tends to cause a decrease of capillary and of venous pressure

POISSEULLE S LAW As blood flows along a vessel, the pressure within the vessel falls The magnitude of the pressure drop depends upon the velocity of the blood flow and upon the resistance to blood flow which is inversely related to the size of the vessel the faster the flow, the greater the pressure drop and the smaller the vessel the greater the pressure drop The major pressure drop in the human circulation occurs in the arterioles which have the narrowest total cross sectional diameter

The relationships between mean pressure peripheral resistance, and blood flow are expressed by Poisseulle s law which states that the rate of flow through a blood vessel is directly proportional to the pres sure gradient or difference between the proximal and distal points and inversely proportional to the vascular resistance that is directly proportional to the size of the vessel In the Poisseulle formula the radius of the vessel is raised to the fourth power this implies that a very small change in the diameter of a vessel causes a marked change in the vascular resistance and hence in the rate of flow Although increase of the proximal pressure causes a proportionate increase of the blood flow through the vessel increase of vessel size results in a relatively greater increase of flow This relationship between mean pressure gradient blood flow and peripheral resistance is of funda mental importance in calculating the dimensions of various areas of the human circulatory bed (Chap 2)

VASOMOTOR REGULATION OF LOCAL BLOOD FLOW As mentioned above, flow through any vessel is accompanied by some decrease of the mean blood pressure However the largest drop of pressure oc curs in the small arteries and arterioles in which the resistance to blood flow is the greatest In the lung this vascular resistance is rela tively passive for vasomotor tone appears to play only a small part in the regulation of the size of the pulmonary blood vessels On the other hand the activity of the autonomic nervous system is of para mount importance in regulating the size of the systemic arterioles This is due to the fact that the various organs all supplied by a com mon pressure head need different amounts of blood at different times Vasomotor activity regulates the blood flow to each organ to

DIRECT EFFECT When a *ventricle contracts, it exerts force on the* blood between its walls and the intraventricular pressure rises When it exceeds the arterial pressure, the outflow valves open, and blood flows forward into the aorta or pulmonary artery This causes the pressure in the aorta or pulmonary artery to rise whereupon blood flows *forward through the arterial system at an accelerated rate* At the end of ventricular contraction the continuing flow of blood out of the arteries causes the arterial pressure to drop At any instant the pressure in the arteries is dependent upon the amount of blood in the arteries and upon the compliance of the arterial walls (see above) Cardiac action increases intra arterial pressure by adding more blood to the arteries with each heart beat

INDIRECT EFFECT Cardiac action also affects the pressure in the circulatory system indirectly Each ventricle operates at a certain filling pressure the atrial pressure (see below Stroke Volume) Impairment of ventricular function is associated with increase of the pressure in the atrium and in all of the veins behind the atrium Normally, the filling pressure of the left ventricle is slightly higher than the filling pressure of the right ventricle so that the pressure in the pulmonary veins is higher than the pressure in the systemic veins

Effect of Peripheral Resistance

So far, it has been pointed out that the pressure in a blood vessel depends upon the amount of blood in that vessel and upon the compliance of the vessel wall The amount of blood in the various vessels is affected directly and indirectly by cardiac action It is also affected by the resistance offered to the flow of blood through the vessel This resistance is caused primarily by the smaller arteries or arterioles If the arterioles are narrowed there is great resistance to the flow of blood out of the arterial reservoir At a given pressure the rate of flow of blood out of the arteries is slower than if the arterioles were dilated As a result the arterial pressure falls less during diastole than it would if the peripheral resistance were less and the mean or average, arterial pressure is higher than it would be if the peripheral resistance were reduced *This also means that less blood and less* pressure is transmitted to the capillaries and to the veins In addition

falls The direct and indirect effects of cardiac action have been mentioned above

Although all these factors may affect the level of the venous pres sure the factor of arterial volume is of little importance since as compared to the volume of blood in the veins, the volume of blood in the arteries is very small Rarely will enough blood be dislocated from the venous system into the arterial system to cause significant reduction of the venous pressure The factors of major importance in determining the magnitude of the venous pressure are the total blood volume the compliance of the walls of the veins and the filling pres sure of the ventricle

EVENTS OF THE CARDIAC CYCLE

Pressure Pulses

So far discussion has centered about the relationships between mean pressure blood flow, and vascular resistance Actually arterial pressure is generated by repetitive contractions of each ventricle and hence is continuously changing Understanding of the normal pres sure waves in the cavities of the heart and great vessels is essential for the interpretation of abnormal patterns that may occur in disease Figure 2 is a classic portrayal of the pressure events in the chambers of the left heart and aorta in relationship to changes in ventricular volume the electrical impulses as registered by the electrocardio gram and the heart sounds during a single cardiac cycle The events in the right heart are qualitatively similar so that discussion and study of this diagram suffices for both ventricles

Spread of the electrical excitatory impulse through the ventricle denoted by the R wave on the electrocardiogram is followed by con traction of the ventricle resulting in a rise of the intracavitary pres sure (isometric contraction) When the pressure in the ventricle exceeds that in the atrium (Fig 2, *1*) the A V valve closes producing the first heart sound and a small rise of pressure in the atrium When *the pressure in the ventricle exceeds that in the aorta* the aortic valve opens (Fig 2 *2*) whereupon blood flows from the ventricle into the aorta During this period the ventricle and aorta are a common cham ber and the pressure in them is identical The fall of atrial and venous pressure during this period is attributed to the downward dis placement of the A V valve serving to enlarge the atrium and to lower the pressure therein thus promoting atrial filling from the

match its metabolic activity Increased oxygen consumption is met by vasodilatation and thus, increased blood flow to the organ No such regional variation of blood flow is necessary in the lung because all of the alveoli have the same function and very limited metabolic needs

PULMONARY ARTERY VERSUS SYSTEMIC PRESSURE Since the circulatory system is a closed one, the right and left ventricles pump identical amounts of blood forward into the pulmonary artery and aorta, respectively Yet the mean pressure in the aorta is about five times as high as the mean pressure in the pulmonary artery, because the systemic arterioles are much narrower than the pulmonary arterioles and offer five times as much resistance to the flow of blood For equal amounts of blood to flow through the two systems, the pressure driving the blood through the narrow systemic arterioles must be five times as high as that driving the blood through the pulmonary arterioles As a result the left ventricle must do approximately five times as much work as the right ventricle

Venous Pressure

The relationships between mean pressure, flow, and volume of blood in the circulatory system are obviously extremely complicated They may be summarized by considering the factors that contribute to the magnitude of the venous pressure

The venous pressure is related both to the amount of blood in the veins and to their compliance Either an increase of venous blood volume or a decrease of venous elasticity leads to an increase of the venous pressure Because blood is flowing through the circulatory system, the amount of blood in the various vessels is not solely dependent upon their compliance Factors that tend to shift blood from the veins into the arterial or capillary systems also tend to reduce venous pressure and vice versa Cardiac action causes blood to be pumped from the venous system into the arterial system The degree to which the venous pressure falls depends upon how much blood is taken from the veins and kept in the arteries This in turn depends upon the compliance of the arteries the arteriolar size and the action of the heart The more compliant the arteries the more blood will they retain Decreased arteriolar size causes increased resistance to the flow of blood out of the arteries and thus the pressure and volume of blood within the arterial system is increased while the venous pressure

venous reservoir The period of ventricular ejection may be divided into rapid (Fig 2 *2–3*) and slow (Fig 2 *3–4*) ejection periods followed by relaxation of the ventricular muscle and abrupt fall of intracavitary pressure When this falls below the aortic pressure the aortic valve snaps shut (second heart sound, Fig 2 *5*), after which further relaxation of the ventricle results in a rapid drop of pressure to a level below that in the atrium This serves to promote early diastolic filling by ventricular suction The onset of ventricular filling (Fig 2 *6*) is coincident with the opening of the A V valve During the remainder of diastole the atrium and ventricle are essentially a common chamber in which the pressure rises as blood enters from the great veins Atrial contraction produces a slight increase of pressure in the two chambers but most of ventricular filling occurs early in diastole (Fig 2, *6–7*) and atrial contraction is a relatively unimportant factor in ventricular filling

The aortic pressure curve reveals an abrupt rise (the incisura) after closure of the A V valves followed by a gentle decline throughout diastole as blood leaves the arterial system through the arterioles This curve declines at an ever slower rate Since the amount of blood leaving the arteries through the arterioles at any time is proportional to the arterial pressure the decline of arterial pressure is associated with a decreased rate of flow The rate of blood flow out of the arterial tree is also dependent upon the peripheral resistance Decreased arteriolar size (vasoconstriction) causes a slower decline of the arterial pressure If uninterrupted by the ensuing heart beat arterial pressure would continue to fall so that the magnitude of the pulse pressure also depends upon the heart rate

The magnitude of the systolic pressure depends on the amount of blood ejected from the ventricle on the level of the pre-existing diastolic pressure and on the distensibility of the aorta The diastolic pressure depends upon how fast the systolic pressure falls and upon the duration of diastole The longer the duration of diastole the lower is the diastolic pressure The rate of fall of pressure depends upon the distensibility of the arterial walls the degree to which the decrease of volume within the arterial system causes a decrease of pressure and upon the peripheral resistance which governs the rate at which blood leaves the arteries Thus the levels of systolic and diastolic pressure are to a large extent interrelated and it is an oversimplification to relate the diastolic pressure to peripheral re

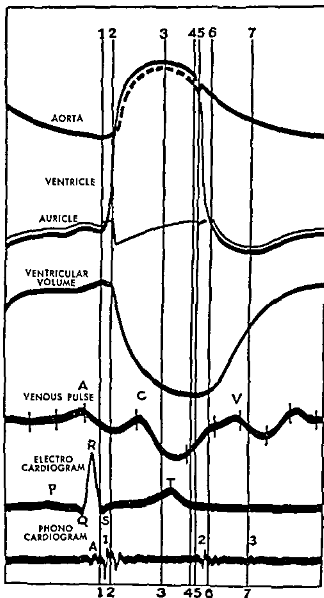


Fig 2 Events of the cardiac cycle From above downward *are depicted the pressures in the aorta ventricle and auricle* (atrium) during a single heart beat Below the pressures are shown the ventricular volume venous pressure electrocardiogram and phonocardiogram

At the onset of ventricular contraction the A–V valve closes *(1)* The aortic valve opens at *(2)* followed by the maximal injection phase (2–3) and the reduced ejection phase (3–4) The aortic valve closes at (5). The A–V valve opens at (6) followed by the phase of rapid ventricular filling (6–7) (From Hoff in Fulton *Textbook of Physiology* ed 17 Philadelphia Saunders 1955)

cardiac output is basic to an understanding of the relationships between oxygen uptake and blood flow The Fick principle states that the oxygen uptake the amount of oxygen taken up by the lungs or used by the tissues is equal to the amount of oxygen entering the lungs or tissues minus the amount of oxygen leaving the lungs or tissues In the case of the tissues for example the amount of oxygen entering equals the cardiac output times the arterial oxygen content The amount of oxygen leaving equals the cardiac output times the venous oxygen content The oxygen uptake by the tissues equals the amount of oxygen which enters minus the amount of oxygen which leaves This equals the cardiac output times the difference between arterial oxygen content and the venous oxygen content (the arterio venous oxygen difference) Tissue oxygen requirements are subserved both by the blood flow and by the arteriovenous oxygen difference The latter is a measure of the amount of oxygen that the tissues extract from the blood flowing through them The cells can get more oxygen if the blood flow increases or if they extract more oxygen from each unit of blood flowing through them Calculation of cardiac output requires measurement of oxygen uptake and of the amount of oxygen in arterial and in mixed venous blood

Heart Rate

The multiple factors which control cardiac output will not be discussed in detail but the important parameters will be outlined briefly Cardiac output is the product of heart rate and of stroke volume The former appears to be largely under nervous and humoral control It is an important factor in meeting the demands for increased blood flow that occur during muscular exercise Up to a point an increase of the heart rate causes an increase of cardiac output Since most of ventricular filling occurs early in diastole (Fig 2) increase of the heart rate up to about 180 beats per minute causes very little diminution of ventricular filling even though the duration of diastole is shortened Since filling is unimpaired the amount of blood in the ventricle at the end of diastole is normal and stroke volume need not be reduced As a result doubling the heart rate may double the cardiac output

Stroke Volume (Starling Principle)

Stroke volume has been traditionally related since the classic experiments of Starling and Frank, to the length of the ventricular

sistance and the systolic pressure to stroke volume Both are affected though to different degrees, by heart rate, stroke volume, and the size and elasticity of all the components of the arterial and arteriolar bed

Measurement of Arterial Pressure

Modern techniques permit faithful recording of the phasic pressure patterns in all of the chambers of the heart and in the large vessels Such techniques as discussed later may provide valuable clinical information Generally, the levels of systolic and diastolic pressure in the arterial system can be assessed with sufficient accuracy by the auscultatory technique This involves inflation of a cuff around the brachial artery and auscultation over the artery distal to the cuff as the pressure in the cuff falls When the level of pressure in the cuff falls lower than the systolic pressure in the artery blood flows through the artery during systole Since the vessel is still partially occluded the blood flow is not streamlined but turbulent and hence noisy Thus the cuff pressure coincident with the appearance of sound over the artery is equivalent to the systolic pressure in the artery When the pressure in the cuff falls lower than that in the vessel at the end of diastole so that the vessel is no longer occluded at all the flow through the vessel becomes streamlined and silent The point of disappearance or sudden change of sound over the artery is therefore equivalent to the diastolic pressure

This is the mechanism of production of the Korotkow sounds used in the clinical estimation of the blood pressure If the arm is excessively obese some of the pressure in the cuff may not be transmitted to the underlying artery with the result that a falsely high level of blood pressure is measured In such cases a wider cuff may be used Alternatively arterial puncture and direct registration of the arterial pressure pulse may be used for accurate measurement of the blood pressure

OXYGEN UPTAKE AND CARDIAC OUTPUT

Fick Principle

Measurements of pressure and flow in the cardiovascular system are basic tools for the study of circulatory function The techniques used for these measurements are beyond the scope of this discussion but an understanding of the Fick principle for measurement of

much more stroke work for a given degree of stretch than the right The stroke volume of the two ventricles is identical, and the end diastolic pressure in the left ventricle is only slightly higher than that in the right Yet the left ventricle pumps blood against a re sistance some five times greater than that met by the right ventricle so that its stroke work is much greater

Myocardial hypertrophy may alter the relationship between fiber length and stroke work For example the right ventricle may be come more like the left in pulmonary hypertension The relationship between stroke work and end diastolic fiber length may also be altered by drugs or by nervous or humoral stimuli During muscular exercise ventricular work may be greatly increased without measur able change of end diastolic pressure (Chap 13) These phenomena have been expressed by Sarnoff as a series of ventricular function curves a different Starling curve being described by the ventricle under different conditions This will be discussed in more detail in Chapter 4

SUBDIVISIONS OF PULMONARY FUNCTION

The end result of pulmonary function is to provide circulating blood with oxygen and to remove carbon dioxide Pulmonary func tion may be subdivided into (1) ventilation of the alveoli (2) dif fusion of gases across the alveolar walls into the blood and (3) distribution of blood and gas flows to similar areas of the lung

VENTILATION AND LUNG VOLUMES

The Alveolar Air

The lung pump is basically different from the heart pump in that air is pumped back and forth through one airway into and out of a large alveolar space While oxygen is continually removed from the alveolar air by venous blood and carbon dioxide is continually added to the alveolar air fresh air rich in oxygen and containing almost no carbon dioxide is added only intermittently to the alveoli Thus there is a small cyclical change in alveolar gas composition during the respira tory cycle During inspiration the alveolar gas composition becomes more like the composition of inspired air higher in oxygen lower in carbon dioxide during expiration when gas exchange continues but

muscle fibers at the beginning of systole As in other muscles, the force of ventricular contraction depends, up to a limit on the degree to which the muscle is stretched A spring behaves in the same fashion—the more it is stretched the more powerful is its tendency to return to the original position Since the force of ventricular contraction or stroke work is the product of stroke volume and the pressure generated by that heart beat stroke volume is directly related to the diastolic length of the myocardial fibers

Many aspects of cardiac function can be understood in the light of the Starling relationship It insures that the stroke outputs of the two ventricles remain identical, despite the fact that the ventricles are separated by capacious vascular beds If for example, the right ventricle began pumping larger quantities of blood than the left, an increased volume of blood would flow into the left ventricle during diastole This would cause an increase of the end diastolic volume of the left ventricle and, hence, a more forceful contraction and an increase of stroke volume Reduction of the output of one ventricle would have the reverse effect

The Starling relationship also explains how a ventricle can intrinsically adapt to a stress If a ligature is tightened around the aorta, ejection of a given amount of blood will require an increase of stroke work During the heart beat after placement of the occluding band the ventricle will do as much stroke work the product of stroke volume and pressure as was dictated by its previous end diastolic size As a result stroke volume will be less than on the previous beat This will result in an increase of the amount of blood in the ventricle at the beginning and hence at the end of the next diastolic period, so that on the next beat the ventricle will contract more forcefully This automatic compensation for varying work loads is accomplished by an increase of the diastolic volume of the ventricle

The relationship between pressure and volume within the ventricle, ventricular distensibility is not well defined but large increases of volume are associated with an increase of pressure A ventricle working harder than normal, either because of increased resistance to flow or because of excessive demands for flow, generally has an elevated end diastolic pressure

The relationship between end-diastolic fiber length and stroke work is vastly different for each ventricle The left ventricle does

Thus the large alveolar volume has the function of buffering the cyclical changes in alveolar gas composition which would otherwise occur, so that there is a relatively constant composition of air in the alveoli The events of a respiratory cycle in terms of alveolar gas composition and volume are shown schematically in Figure 3

Subdivisions of Lung Volume

The subdivisions of lung volume are shown in Figure 4 The total lung capacity the volume of air in the lungs after a maximal inspiration may be divided into two components the vital capacity and the residual volume The vital capacity is the total volume of air that can be blown out of the lungs with a maximal expiration after a full inspiration The residual volume is the amount of air left in the lungs after a maximal expiration

Lung volumes may also be categorized on the basis of the normal respiratory cycle The amount of air left in the lungs after a normal expiration is the functional residual capacity (FRC) This consists of air that can be blown out of the lungs by forced expiration the expiratory reserve volume and the residual volume The inspiratory

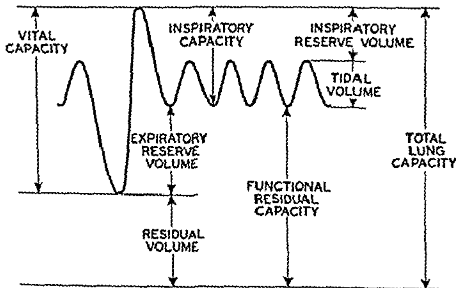


Fig 4 Subdivisions of lung volume The tidal volume may be increased by encroachment on either the inspiratory reserve volume or the expiratory reserve volume The sum of these three volumes is the vital capacity which along with the air left in the lung after a maximum expiration the residual volume makes up the total lung capacity

the alveoli are not being diluted with inspired air, the alveolar CO_2 increases and the O_2 falls Great cyclical changes of alveolar gas composition do not occur because the alveolar gas volume is large and the volume of gas exchange across the alveoli during the course of a breath is insufficient to distort it a great deal The volume of fresh air entering the alveoli during a single breath is likewise too small to effect much change in the composition of the alveolar air

$\dot{V}CO_2$ $\dot{V}O_2$ 300cc/MIN — f = 10

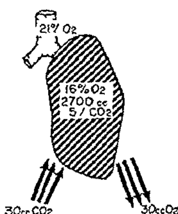
$V CO_2$ 30 $V O_2$ — V_T 700cc

$\dot{V}_A$ 600cc — V_D 100cc

R 1

END EXPIRATION — END INSPIRATION — END EXPIRATION







V_{ACO_2}	100	135	100
V_{AO_2}	320	432	320

Fig 3 Events of the respiratory cycle Schematic illustration of the events occurring during the course of a respiratory cycle depicted as if CO_2 entered the alveoli and O_2 was removed at the same time as the alveoli were filled with air The diagram is drawn for a normal subject with an oxygen consumption and CO_2 production ($\dot{V}CO_2$) both equal to 300 cc/min or 30 cc per breath since the respiratory rate is 10 The tidal volume (V_T) is made up of air going into the alveoli (V_A) and air going through the dead space (V_D) At the end of inspiration the increase of alveolar volume with fresh air (V_A) is balanced by O_2 uptake and CO_2 production so that the alveolar gas composition is unaltered Some fresh air remains in the dead space (stippled area) After expiration the entire lung is filled with alveolar gas In reality ventilation is intermittent whereas CO_2 production and O_2 uptake are continuous This tends to cause cyclic fluctuation of the alveolar gas composition which is minimized by the large size of the alveolar space relative to tidal volume and to metabolic rate

pressure in the alveoli and air flows in from the mouth The reverse occurs during expiration

The velocity of airflow is inversely proportional to the size of the airways Just as in the case of blood flow through the vessels (see above Poisseulle s Law) the rate of airflow through the airways is rapid when the airways are large in diameter slow when the air ways are small If airflow is to be sufficiently rapid to provide adequate alveolar ventilation the airways must be widely patent By utilizing the principle that the velocity of airflow is directly dependent upon the pressure gradient along the airways and inversely pro portional to the size of the airways the size of the tracheobronchial tree may be assessed (Chap 2)

LUNG STIFFNESS In addition to developing pressure in order to generate airflow along the airways the respiratory muscles must also develop pressure to stretch the lungs The lung compliance is a measure of the distensibility of the lungs It is defined as the volume change produced by 1 cm H O pressure Inflation of the lung requires an increase of the thoracic volume When the lungs are inflated they tend to pull inward from the chest wall so that the pressure in the potential space between the chest wall and lung (pleural pressure) falls This can be approximately measured by an esophageal balloon technique The increase of lung volume divided by the corresponding fall of pleural pressure equals the lung compliance This measurement provides an objective index of lung stiffness (Chap 2)

Alveolar Ventilation and Alveolar Gas Composition

The end result of ventilatory function is the maintenance of normal alveolar gas composition expressed most conveniently as a partial pressure of carbon dioxide of about 40 mm Hg and of oxygen of about 100 mm Hg This in turn depends upon two factors (1) the metabolic rate expressed either as the volume of carbon dioxide added to the alveoli per minute or as the volume of oxygen taken out and (2) the volume of air entering and leaving the alveoli per minute the alveolar ventilation These relationships are depicted in Figure 5 Excessive alveolar ventilation results in a low alveolar carbon dioxide tension ($P_{A_{CO}}$) and a high alveolar oxygen tension (P_{A_O}) The re verse occurs in hypoventilation Increase of the metabolic rate tends to cause an increase of the alveolar P_{CO} and a decrease of the alveolar

capacity is the amount of air that can be inspired into the lung after a normal expiration, and it is made up of the tidal volume, the volume of a normal inspiration, plus the inspiratory reserve volume

Functionally, the two important volumes are the FRC and the tidal volume The FRC is large relative to the tidal volume so that phasic additions of inspired air to the FRC have little effect on alveolar gas composition (see above) The tidal volume is the amount of air that actually goes in and out of the lung Some of this air, about one third goes in and out of the air conducting passageways the anatomical dead space The rest goes into the alveoli to provide them with fresh air to counterbalance the continuous oxygen uptake and carbon dioxide production This is the air that provides the alveolar ventilation, the major purpose of ventilatory function

Mechanics of Respiration

The act of ventilation is dependent upon (1) the bellows action of the chest (2) the patency of the airways through which air must pass to the alveoli and (3) the compliance, or distensibility, of the lungs

BELLOWS ACTION OF THE CHEST The bellows action of the chest involves enlargement of the thoracic cage during inspiration and con traction during expiration Inspiration is an active process, whereas expiration is largely passive During inspiration expansion of the chest causes the lungs to expand so that air flows into the alveoli Contraction of the chest and lungs during expiration causes air to flow out of the alveoli The effectiveness of this bellows action de pends upon the strength and innervation of the respiratory muscles including the diaphragm and upon the movement of the ribs, in turn dependent upon the structural integrity of the bones and joints of the thorax

PATENCY OF AIRWAYS The flow of air through the airways is governed by forces similar to those that influence the flow of blood through the vessels The velocity of airflow is directly proportional to the pressure gradient from the alveoli to the mouth This pressure gradient is positive during expiration negative during inspiration It is generated by the bellows action of the chest wall When the chest enlarges, the intra alveolar pressure falls so that there is negative

150 cc, and if he breathes 10 times per minute, his dead space ventilation is 1500 cc per minute His total ventilation must then be 5500 cc per minute However, if he breathes 20 times a minute, his dead space ventilation is now 3000 cc per minute and his total ventilatory requirement is 7000 cc per minute He has to move an additional 1500 cc of air in and out of his dead space when he doubles his respiratory rate

At increasing respiratory rates ventilation of the dead space involves an increasing percentage of the total ventilation Thus one may pant 40 times a minute and actually suffer from alveolar hypoventilation because most of the small tidal volume simply goes in and out of the dead space

DIFFUSION

The second step in pulmonary function is the diffusion of oxygen and carbon dioxide across the alveolar walls Since carbon dioxide is more than 20 times as diffusible as oxygen, carbon dioxide retention from impaired diffusion is rarely, if ever a problem On the other hand hypoxemia may result from impaired diffusion of oxygen This function will be considered in terms of the diffusion of oxygen

Since diffusion is a physical process, the amount of oxygen that diffuses across the alveoli in a unit of time depends upon the pressure head of oxygen available for diffusion just as the rate of flow of gas or liquid through tubes depends upon the pressure head of the gas or liquid The pressure head for diffusion of oxygen is the alveolar oxygen tension which has been discussed above Elevation of the alveolar oxygen tension causes accelerated diffusion of oxygen into the alveolar capillary blood and reduction of the alveolar oxygen tension causes decrease of the rate of diffusion of oxygen

Diffusing Capacity

The rate of diffusion of oxygen also depends upon the area and the thinness of the diffusion surface the alveolar-capillary membrane The larger and thinner the alveolar-capillary membrane the more rapid the rate of diffusion of oxygen Thus the diffusing capacity of the lungs is a measure of the effective size and thinness of the alveolar-capillary surface and it is defined as the oxygen uptake per minute (the rate of diffusion) divided by the pressure gradient for oxygen across the alveoli The normal alveolar capillary mem

P_{O_2} Changes in metabolic rate are generally matched by a corresponding change of the alveolar ventilation, and so the alveolar gas composition is not altered In muscular exercise, for example, a marked increase in the metabolic rate is accompanied by a parallel increase in the alveolar ventilation and the alveolar gas composition does not change

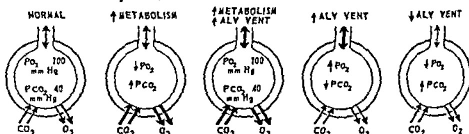


Fig 5 Relationship between alveolar ventilation the metabolic rate (expressed as either oxygen uptake or as carbon dioxide production) and alveolar gas composition Alveolar oxygen tension (P_{O_2}) varies directly with alveolar ventilation and inversely with oxygen uptake Alveolar carbon dioxide tension (P_{CO_2}) varies inversely with alveolar ventilation and directly with carbon dioxide production

Regulation of the alveolar ventilation is accomplished by the respiratory center By regulating the rate and depth of total ventilation, the respiratory center effects adjustment of the alveolar ventilation so as to maintain a constant alveolar gas composition in the face of a changing metabolic rate

Dead Space Ventilation

The total ventilation consists of the alveolar ventilation plus the amount of air that goes in and out of the tracheobronchial tree the dead space The dead space ventilation equals the volume of the dead space times the respiratory rate With each breath a certain amount of inspired air goes in and out of the tracheobronchial tree At faster respiratory rates the dead space ventilation becomes greater so that a smaller proportion of the total ventilation gets in and out of the alveoli and ventilation becomes less efficient This can be illustrated by an example Suppose that a man requires an alveolar ventilation of 4000 cc per minute If his dead space has a volume of

DISTRIBUTION

Finally, normal arterial blood gas-composition the end result of pulmonary function requires that both blood and gas go to similar areas in the lung Each alveolus must receive proportionate amounts of circulation and of ventilation Areas that are well ventilated receive correspondingly more blood, and poorly ventilated alveoli are poorly perfused This means that the ratio of ventilation to perfusion is the same in each alveolus

Ventilation Perfusion Ratios

The concept of ventilation perfusion ratios may best be understood if one examines the consequences of different ventilation perfusion ratios in two parts of the lung In Figure 7 one lung receives less ventilation than the other but they each receive the same amount of blood When ventilation is reduced with respect to blood flow the oxygen consumption and carbon dioxide output of the blood

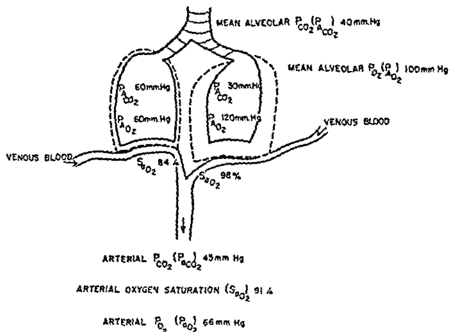


Fig 7 Impa ment of distr but on when one lung ecei es less ventilation tha the othe but both receive sim lar quantit es of blood flow Altho gh the alveolar gas compos t on is normal because the average alveolar vent lat on is normal the e is hypoxem a and ca bon d o ide ret nt on in the arterial blood Th s is due to the fact that the two l ngs have d fferent ventilat on perfus on rat os

brane is extensive and thin The diffusing capacity is so high that oxygen diffuses across the alveolar capillary membrane so rapidly that the venous blood entering the alveolar capillary takes up its full quota of oxygen long before it reaches the end of the alveolar capillary Blood traversing the alveolar capillary attains an oxygen tension equal to that in the alveolus early in its course along the capillary whereupon diffusion ceases (Fig 6*A*) When the diffusing capacity is reduced (Fig 6*B*), oxygen diffuses much more slowly with the result that the blood never becomes fully saturated with oxygen Diffusion continues as the blood traverses the entire length of the alveolar capillary, and yet the oxygen tension of the blood leaving the alveolus is lower than the alveolar oxygen tension The normal diffusing capacity is so large that even when the oxygen uptake is increased tenfold as in heavy muscular exercise the blood still leaves the alveolar capillaries at an oxygen tension practically indentical to that in the alveoli

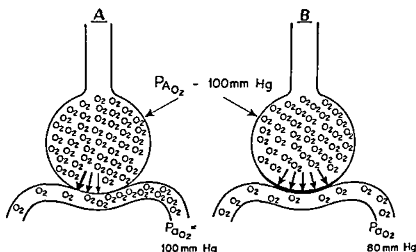


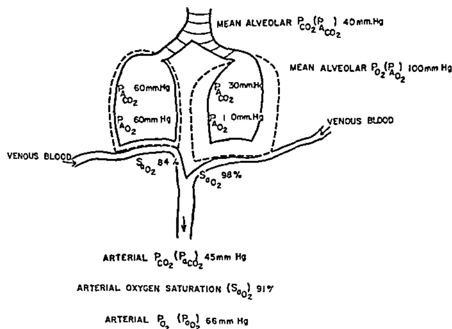
Fig 6 Schematic illustration of diffusion of oxygen from alveolus into capillary blood The rate of diffusion depends upon the difference between the partial pressure of oxygen in the alveolus ($P_{A_{O_2}}$) and in the blood and upon the size and thinness of the surface area available for diffusion The latter is so large and so thin that normally oxygen diffuses very rapidly across the alveolar capillary membrane As the oxygen tension rises in the blood traversing the alveolar capillary the rate of diffusion becomes correspondingly slower Nevertheless blood leaves the normal alveolus (A) at an oxygen tension (P_{O_2}) identical to the alveolar P_{O} When the diffusing capacity is reduced (B) the rate of diffusion is so slow that the oxygen tension in the blood never rises as high as the oxygen tension in the alveolus so that diffusion continues along the entire length of the alveolar capillary

DISTRIBUTION

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F g 7 Imp m t of d t b t o wh o e lung ece v less ve t lat o than th oth but both r e m la qua tit of blood flow Although the al olar gas compo t o is o mal b au th a erage al ol v t l t o is no mal ther hypo m a and ca bon d o d tent n the art al blood Th is due to th fact that the two l gs hav d ffe ent v t lat o p rfus on rat os

are not matched by enough alveolar ventilation. The alveolar oxygen tension falls and the P_{CO_2} rises. The reverse occurs when the ventilation is greater than the blood flow. Since the ventilation-perfusion ratio is relatively low in the right lung, its carbon dioxide tension is elevated and the oxygen tension is reduced. The opposite is the case in the left lung. The oxygen saturation of the blood leaving each lung is determined by the alveolar oxygen tension and by the oxygen dissociation curve. The lower alveolar oxygen tension in the right lung causes the oxygen saturation of its blood to be reduced. There is no corresponding elevation of the oxygen saturation of the blood leaving the left lung, since the oxygen dissociation curve is such that elevation of the alveolar oxygen tension above 100 mm Hg causes little increase of the oxygen saturation of the blood. As a result, the average arterial oxygen saturation (Sa_{O_2}) of the mixture of blood from the two lungs is reduced to 91 per cent. Carbon dioxide retention, defined as an arterial P_{CO_2} which is higher than the average alveolar P_{CO_2}, is also present.

In the normal lung there is undoubtedly some regional variation of ventilation. Some alveoli get more air than others. Hypoxemia and carbon dioxide retention are prevented by compensatory adjustment of blood flow so as to maintain a normal ventilation-perfusion ratio. In areas in which ventilation is poor, perfusion is reduced, whereas well ventilated alveoli receive a great deal of blood. This adjustment may be mechanical in that the capillaries lining well ventilated alveoli may be opened and closed by inflation and deflation and thus pump a great deal of blood. The capillaries lining collapsed alveoli may also be collapsed so that there is no perfusion in these nonventilated areas. In addition, hypoventilation causes reduction of the alveolar oxygen tension. This may cause local vasoconstriction, thus reducing perfusion and restoring the ventilation-perfusion ratio toward normal.

Intrapulmonary Distribution of Inspired Air

Normally, inspired air is distributed fairly evenly throughout the entire lung. As a result, if one breathes pure oxygen, the nitrogen in the lungs is washed out fairly rapidly. After 7 minutes the air in the lungs contains less than 2 per cent nitrogen. If inspired air is distributed poorly throughout the lungs, the washout of nitrogen from hypoventilated areas is greatly delayed. Nitrogen washout curves

provide one method for testing the intrapulmonary distribution of inspired air

Lung mixing may also be tested by the continuous measurement of the expired carbon dioxide concentration during a single expiration The first portion of the expiration consists of dead space air in which the CO_2 concentration is nearly zero This is followed by a rise of CO_2 concentration, as the dead space is flushed out, to a plateau of about 6 per cent All the air is now coming from the alveoli and the alveolar carbon dioxide concentration remains constant If the lung is ventilated unevenly there will never be a plateau on the CO_2 expirogram The concentration of carbon dioxide will rise continuously as air is forced out of the poorly ventilated areas which contain higher concentrations of carbon dioxide As expiration continues the emptying alveoli are more and more those that received the least ventilation, and so the CO_2 content of the expiration rises to higher and higher levels

REFERENCES

ANKENEY J L, FISHMAN A P and FRITTS H W JR. An analysis of normal and abnormal left atrial pressure pulse in man *Circulation Res* 4 95 1956

ARNOTT W M Order and disorder in pulmonary function *Brit M J* 2 279 1955

BRECHER G A *Venous Return* Grune & Stratton 1956

COMROE J H JR FORSTER R E DUBOIS A B BRISCOE W A and CARLSEN E *The Lung* Chicago Year Book Publishers 1955

DUBOIS A B and MARSHALL R Measurements of pulmonary capillary blood flow and gas exchange throughout the respiratory cycle in man *J Clin Invest* 36 1566 1956

FENN W O Mechanics of respiration *Am J Med* 10 77 1951

FORSTER R E Exchange of gases between alveolar air and pulmonary capillary blood pulmonary diffusing capacity *Physiol Rev* 37 391 1957

FREIS E D and ROSE J C The sympathetic nervous system the vascular volume and the venous return in relation to cardiovascular integration *Am J Med* 22 175 1957

GORDON B L Ed *Clinical Cardiopulmonary Physiology* New York Grune & Stratton 1957

GREGG D E SABISTON D C and THEILEN E O Performance of the heart changes in left ventricular end diastolic pressure and stroke work during infusion and following exercise *Physiol Rev* 35 130 1955

KATZ, L N Analysis of the several factors regulating the performance of the heart *Physiol Rev* 35 91 1955

LILLIENTHAL J L JR and RILEY R L Diseases of respiratory system circulation through the lung and diffusion of gases *Ann Rev Med* 5 237 1954

OTIS A B The work of breathing *Physiol Rev* 34 449 1954

RUSHMER R F *Cardiac Diagnosis* Philadelphia Saunders 1955

RUSHMER R F Anatomy and physiology of ventricular function *Physiol Rev* 36 400 1956

SARNOFF S J Myocardial contractility as described by ventricular function curves *Physiol Rev* 35 107 1955

SARNOFF S J and BERGLUND E Ventricular function 1 Starling s law of the heart studied by means of simultaneous right and left ventricular function curves in the dog *Circulation* 9 706 1954

WIGGERS C J *Circulatory Dynamics* Grune & Stratton 1952

WILLIAMS M H JR Experimental alteration of pulmonary function *Dis Chest* 32 656 1957

CHAPTER 2

EVALUATION OF STRUCTURE BY PHYSIOLOGICAL TECHNIQUES

One aim of physiological study of the cardiorespiratory system is to obtain information about the structure of the system Knowledge of structural abnormality is a cornerstone to the evaluation of many patients but it is also necessary to decide what bearing structural abnormality has on a patient s signs symptoms and prognosis This may be difficult For example it is frequently hard to determine whether or not valvular stenosis of a known degree represents such a threat immediate or future to a patient s existence that its surgical correction should be attempted

This chapter sets forth some of the areas in which physiological investigation provides delineation and quantitation of abnormalities of structure Such assessment is only a part of the evaluation of a patient It behooves the physician to evaluate and to treat in the light of symptoms and known facts about the natural history of disease rather than solely on the basis of the extent of a given abnormality

OBSTRUCTION TO THE CIRCULATION

Structural narrowing of the circulatory system may occur at one of the four heart valves in the pulmonary arterioles in the systemic arterioles or in a single blood vessel The natural history and symptoms of disease at each site are vastly different but quantitative assessment of the degree of obstruction at any site is based on the same principle—that the degree of obstruction is proportional to the pressure drop across the area (pressure gradient) divided by the blood flow As pointed out in Chapter 1 (Poisseulle s Law) the

magnitude of the pressure gradient (the mean pressure proximal to the obstruction minus the mean pressure distal to the obstruction) varies directly with the degree of obstruction The pressure gradient also varies directly with the magnitude of the blood flow Thus accurate assessment of the degree of circulatory obstruction requires measurement of the pressure on each side of the obstruction and of the amount of blood flow through it In some instances, a value may be assumed for the distal pressure without introducing too much inaccuracy Each of the four sites of structural narrowing will now be considered separately

Tricuspid Stenosis

The least frequently encountered of the valvular stenoses this lesion is readily assessed by right heart catheterization Quantitation of valve area requires simultaneous measurement of right atrial and right ventricular pressures and cardiac output Valve area is estimated by dividing the mean flow rate during diastole by the mean pressure gradient in diastole (during which all the flow occurs) (Fig 8) When tricuspid stenosis is mild the pressure gradient across the valve may be so small as to escape detection when the blood flow is normal When the cardiac output is increased by muscular exercise, a larger measurable gradient may develop, and then the valve area may be calculated Thus it may be necessary to study the patient during exercise in order to detect and measure the valve area accurately

Pulmonic Stenosis

Evaluation of pulmonic stenosis requires measurement of the pressure gradient across the pulmonic valve during systole, since blood flows across this valve only during the period of ventricular ejection (Fig 8) Valve area is assessed by dividing the mean systolic flow rate by the pressure gradient Since pulmonic stenosis is generally sufficiently severe to result in a pressure gradient at low levels of blood flow exercise measurements are rarely required for assessment of this lesion

The high level of pulmonary artery flow present in some patients with a left to-right shunt due to an atrial or ventricular septal defect may cause a measurable pressure gradient in the absence of severe stenosis This emphasizes the need for knowledge of the rate of blood flow through the valve if one is to interpret a pressure gradient correctly and to calculate valve area

It is of some importance to the surgeon to know whether pulmonic stenosis is of the valvular or infundibular type Angiocardiographic studies may provide this information by actually outlining the area of narrowing One may also obtain data by measurement of the pressure at the end of the cardiac catheter as it is observed to pass from the pulmonary artery to the right ventricle If the pressure

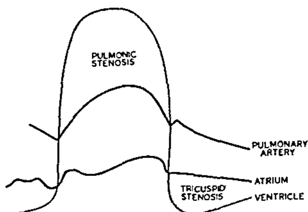


Fig 8 Schematic illustration of the systolic pressure gradient between the right ventricle and the pulmonary artery in pulmonic stenosis and of the diastolic pressure gradient between the right atrium and right ventricle in tricuspid stenosis Similar gradients develop in the left heart in aortic and mitral steno

changes abruptly as the catheter is drawn backward a short distance in the neighborhood of the pulmonic valve valvular stenosis is probably present A gradual rise of pressure or a region of moderate elevation of systolic pressure as the catheter passes from the area of the pulmonary valve into the right ventricle suggests the presence of infundibular stenosis A small infundibular stenosis particularly if located high in the ventricular outflow tract may easily be mistaken for valvular stenosis

Mitral Stenosis

Evaluation of mitral stenosis requires measurements of the diastolic pressure in the left atrium and left ventricle and of the cardiac output Mitral valve area is assessed by dividing the diastolic flow rate by the pressure gradient The left atrium may be entered by needle puncture through the back or through the anterior chest wall through a bronchoscope or recently through the atrial septum from a catheter in

the right atrium A catheter may then be threaded through the needle into the left ventricle, or the left ventricle may be punctured directly through the anterior chest wall

Another approach to the evaluation of left atrial pressure is afforded by the "wedge pressure This is obtained by wedging a cardiac catheter inserted into the pulmonary artery by the conventional technique, into a distal branch of the pulmonary artery Under these circumstances no blood flows by the catheter, and the pressure measured at the tip reflects the pressure in the pulmonary capillaries presumably the next vascular bed through which blood is flowing downstream from the wedged catheter Unfortunately the validity of this measurement as an index of left atrial pressure is open to some question and in order to calculate the mitral valve area one must subtract an assumed value for left ventricular end diastolic pressure Although the level of wedge pressure may be a useful reflection of left atrial pressure calculation of mitral valve area from this measurement is of dubious accuracy

Aortic Stenosis

Assessment of aortic stenosis involves measurement of the left ventricular systolic pressure and of the systolic pressure in any peripheral artery since the pressure in the aorta is not significantly different from that in its peripheral branches Valve area is estimated by dividing the systolic flow rate by the pressure gradient Left ventricular pressure may be measured by direct puncture of the ventricle or by passage of a small catheter through a needle in the left atrium As in pulmonic stenosis, exercise studies are rarely required for accurate evaluation of this lesion since clinically significant aortic stenosis is almost always associated with a measurable systolic pressure gradient across the aortic valve even if the cardiac output is reduced

Increased Pulmonary Vascular Resistance

The major resistance to the flow of blood through the lungs is in the pulmonary arterioles The size of the pulmonary arteriolar bed is reflected in the magnitude of the pressure in the pulmonary artery the smaller the bed the higher the pressure Accurate assessment of pulmonary arteriolar resistance requires simultaneous measurement of the pressure distal to the pulmonary arterioles the pulmonary capillary pressure the pressure proximal to the arterioles the pulmonary artery pressure, and blood flow The last two measurements are relatively

simple to obtain and the pulmonary capillary pressure may be meas ured either from the left atrial pressure at left heart catheterization or from the wedge pressure

Since the pulmonary capillary pressure rarely rises above 30 mm Hg severe pulmonary hypertension may be ascribed to increased pulmonary arteriolar resistance Thus measurement of the pulmonary artery pressure alone provides a rough guide to the flow capacity of the system Severe pulmonary hypertension implies a restricted pul monary vascular bed As is the case with valvular obstruction the pressure also depends upon the magnitude of the blood flow Moderate degrees of pulmonary vascular narrowing may be associated with a normal resting pressure in the pulmonary artery but may be revealed by abnormal elevation of the pressure in the pulmonary artery during muscular exercise A normal pulmonary artery pressure during exer cise indicates that the pulmonary vascular bed is not restricted

Increased Systemic Vascular Resistance

Quantitation of systemic vascular resistance requires simultaneous measurement of blood flow mean arterial pressure and mean right atrial pressure A value for the latter is usually assumed Accurate measurement of mean arterial pressure requires an arterial puncture but a value equal to one third the pulse pressure plus the diastolic pressure is frequently used Since the mean arterial pressure is much higher than the mean capillary pressure an erroneous assumption of a value for the right atrial pressure has little effect on the calculated vascular resistance

Although systemic hypertension is generally the result of increased peripheral (arteriolar) resistance the level of blood pressure is also dependent upon the magnitude of the systemic blood flow It may be affected by an increase or decrease of cardiac output Many drugs reduce the blood pressure by diminishing the cardiac output and this may not be a desirable therapeutic effect Accurate assessment of the pharmacologic effects of antihypertensive agents requires measure ment of the cardiac output as well as of the mean arterial pressure

VALVULAR INSUFFICIENCY

Although abnormal pressure tracings may suggest the presence of valvular insufficiency accurate diagnosis and evaluation of lesions of this type depend upon the injection of a foreign substance into the

cardiac chamber or vessel distal to the lesion and recovery of that substance from the proximal cardiac chamber in the ensuing few heart beats Thus, tricuspid insufficiency is suggested by a rise of the pressure in the right atrium during ventricular systole It may be diagnosed with assurance only if dye injected into the right ventricle is recovered from the atrium during the next few heart beats Angiocardiographic study, with injection of the contrast medium into the right ventricle, also delineates this lesion The same applies to lesions of the mitral valve and the relationship of mitral insufficiency to the left atrial pressure The contour of the latter, or of the pulmonary wedge tracing may suggest the diagnosis of mitral insufficiency but more elaborate study is necessary for accurate evaluation In the case of aortic and pulmonic insufficiency, a wide pulse pressure in the aorta or pulmonary artery is suggestive of the diagnosis, but recovery of dye or contrast material from the left or right ventricle after injection into the aorta or pulmonary artery is necessary for definitive diagnosis Since pulmonic insufficiency is generally a result of prolonged pulmonary hypertension, a normal pressure in the pulmonary artery tends to exclude this diagnosis

Dye Dilution Curves

Dye dilution curves are becoming increasingly useful in the evaluation of abnormalities of the circulation Such curves are obtained by injecting a bolus of dye into the circulation at a known site and analyzing the blood at some distal point for its concentration of the material injected (Fig 9) As mentioned above precise delineation of many lesions is afforded by injection into one cardiac chamber and sampling from another Useful information is also provided by injection into various chambers and sampling from the arterial system When dye is injected into the right atrium it appears in the arterial system in about 8 seconds (Fig 9 *3*) The concentration of dye rapidly rises to a peak (Fig 9 *4*) and then gradually falls About 20 seconds after injection more dye reaches the sampling needle after completing one circulation and the concentration rises again (Fig 9 *5*)

These curves are particularly helpful in the evaluation of right to left shunts but abnormal curves are also obtained from individuals with a large degree of valvular insufficiency Dye injected into the chamber just downstream from the insufficient valve or into any

chamber upstream appears at the point of sampling in a normal time or somewhat early But some dye goes backward with regurgitated blood at each heart beat Because of this, the peak concentration of dye is low and delayed The disappearance curve is likewise delayed and the recirculating dye may not cause a detectable second peak

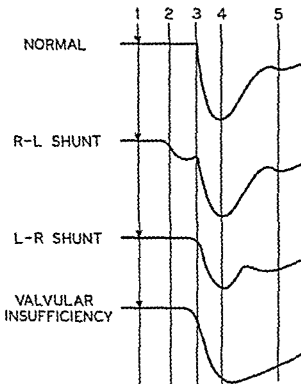


Fig 9 Schematic illustration of dye dilution curves obtained in normal subjects and in patients with central shunts or valvular insufficiency In right to left (R-L) shunts some of the dye injected at (1) appears early at the sampling site (2) the rest appearing normally at (3). Peak concentration is reached at (4) followed by disappearance of the dye and then recirculation at (5) In left-to-right (L-R) shunts the disappearance curve is interrupted early by the recirculating dye and in valvular insufficiency the disappearance portion (4-5) is greatly delayed and does not show the normal recirculation peak (5).

The degree of abnormality of the curve reflects the severity of the valvular insufficiency

If injections are made at multiple sites dye curves may also be used to determine which valve is insufficient Only when the dye is

actually regurgitated does an abnormal curve result If injection is made into a chamber beyond that containing an insufficient valve the curve is normal The most proximal chamber into which injection results in a normal curve is just distal to the chamber containing an insufficient valve Thus, in mitral insufficiency an abnormal curve is usually obtained when dye is injected into the left ventricle and all chambers back of it and a normal curve is seen after injection into the aorta In aortic insufficiency dye injected into all of the cardiac chambers produces an abnormal curve

SHUNTS

Blood may flow in either direction through a shunt The direction depends on the pressure on either side Thus, when pulmonary hyper tension develops the usual left to right shunt through a patent ductus arteriosus becomes bidirectional and then entirely from right to left when the pulmonary pressure exceeds the aortic pressure Increased pulmonary blood flow from any type of central shunt may lead to pulmonary hypertension with eventually, reversal of the direction of flow

An intracardiac communication may be detected by direct passage of a cardiac catheter through it When this cannot be done the diag nostic technique selected for localization of the opening depends upon the direction of the blood flow through it

INTRACARDIAC LEFT TO RIGHT SHUNTS

Oxygen Step up

Left to right shunts are diagnosed and quantitated by measurement at cardiac catheterization of the oxygen content of the blood in the chambers of the right heart and pulmonary artery Normally the oxygen saturation is the same in the blood in the right atrium right ventricle and pulmonary artery A left to right shunt mixes oxygen ated blood with the venous blood in the affected chamber Blood in this chamber and in the chambers beyond contains more oxygen than does the mixed venous blood A sudden increase (step up) of the oxygen saturation indicates a left to right shunt at that site In addition to localizing the site of a left to right shunt this technique provides information about its size the larger the shunt the greater the step up The amount of blood which flows through the shunt may

be calculated from knowledge of the oxygen content of the blood on each side of the shunt and in the mixed stream distal to it

The diagnosis of left to right shunts by this technique is subject to two particular errors regarding proper localization of the site of the defect In the first place oxygenated blood may flow in a stream through the involved chamber so that the oxygen saturation of the blood in that chamber is not elevated In such a case the step up may appear in the next chamber For example an atrial defect may be mistakenly diagnosed as a ventricular defect or more commonly a high ventricular defect mistakenly may be thought to be a patent ductus arteriosus In the second place patients with a ventricular defect a large right ventricle and functional tricuspid insufficiency or with patent ductus arteriosus pulmonary hypertension and pulmonary insufficiency may reveal a step up of oxygen saturation in the chamber of the heart proximal to that into which the shunt empties This is due to regurgitation of oxygenated blood through the insufficient valve Both of these errors may be minimized if multiple samples of blood are analyzed for their oxygen content at the time of cardiac catherization

Dye Dilution Curves

Left to right shunts have in common the production of an abnormal dye dilution curve that is not diagnostic as to site but which suggests the presence of a shunt Such a curve is characterized by the appearance of dye in the systemic circulation in a normal time interval or earlier after intravenous injection but because some of the injected dye recirculates rapidly back through the shunt the peak concentration is reduced and the recirculated dye appears early on the disappearance curve (Fig 9) Dye dilution techniques may also be used to detect and localize left to right shunts if dye is injected into one area of the circulation and sampled from another This may be done either by introducing a double lumen catheter into the right side of the heart or by introducing two or more catheters into different cardiac chambers The technique involves injection of dye into the distal chamber and sampling from the proximal one Normally about 15 seconds are required for the dye to circulate through the lungs left side of the heart systemic vascular bed and back to the right side of the heart In the presence of a left to right shunt some of the dye gets back to the right side of the heart much more rapidly

Appearance of dye in the right side of the heart before it appears in a systemic artery indicates the presence of a left to right shunt if there is no insufficiency of the valve separating the injection from the sampling sites In such a case, dye should appear in the proximal chamber immediately after injection into the distal one By injecting into and sampling from several areas, one can ascertain the site of the shunt

An alternative technique involves inhalation of a foreign gas such as nitrous oxide or radioactive iodine, followed by measurement of the concentration of the gas in the blood sampled from either the right atrium or the right ventricle and from a systemic artery This technique is similar in principle to the dye technique but instead of injecting dye into the cardiac chamber distal to the sampling site gas is introduced into the lung capillaries by inhalation Appearance of the gas in a chamber on the right side of the heart sooner than its appearance in the arterial system indicates a left to right shunt at or proximal to that chamber Sampling from several chambers permits localization of the site of the shunt the most proximal chamber showing early appearance of the gas being the one into which the shunt empties This technique has the advantage of requiring passage of only one single lumen catheter into the heart but the instrumentation is a bit more complicated than that employed for dye studies

INTRACARDIAC RIGHT TO LEFT SHUNTS

Systemic Hypoxemia

These lesions cannot be detected by analysis of the oxygen content of the blood in the right side of the heart Since the shunt is from right to left the composition of the venous blood is the same in all the chambers of the right heart On the other hand, some of the venous blood mixes with oxygenated blood returning to the left heart from the lung and thus the arterial oxygen saturation is reduced The degree of systemic hypoxemia is a direct reflection of the size of the shunt

Dye Dilution Curves

A precise method for localizing these shunts is provided by dye dilution curves Dye injected into the chamber containing the shunt, or into an area of the circulation proximal to it will appear abnormally soon in the systemic circulation (Fig 9) This early appearance

is a result of "short circuiting" of some dye from the right to the left side of the heart The magnitude of the early deflection is proportional to the size of the shunt Dye injected into chambers of the heart distal to the shunt appears within a normal period providing localization of the origin of the shunt

PULMONARY AND SYSTEMIC ARTERIOVENOUS FISTULAS

Physiological techniques contribute little to the localization of peripheral communications between the two sides of the circulation However, measurements can be made which have bearing on the size of the shunt through the fistula In pulmonary arteriovenous fistulas the degree of hypoxemia is directly proportional to the size of the right to-left shunt and in systemic arteriovenous fistulas (Chap 5) the magnitude of the shunt is reflected in the level of the cardiac output—the more the flow through the fistula the higher the cardiac output Localization of these lesions is generally made by physical and roentgenographic examination though special techniques such as angiography may be necessary in the case of pulmonary arteriovenous fistulas

OBSTRUCTION OF AIRWAYS

Obstruction of the airways leading from the mouth to the alveoli is assessed in the same way as obstruction to the circulatory pathway To calculate resistance to airflow a measure of the size of the airways it is necessary to measure the pressure at the end of the airways the alveoli the pressure at the beginning of the airways the mouth and the velocity of airflow through the airways Airway resistance is calculated by dividing the pressure gradient from mouth to alveoli by the velocity of airflow The pressure gradient is most easily obtained by taking the mouth pressure as zero and by using the easily measured intraesophageal pressure as a reflection of the intra alveolar pressure The rate of airflow is measured with a pneumotachygraph

Most individuals with narrowing of the airway reveal marked slowing of the rate of airflow from the lungs during expiration Thus even if one does not measure the intraesophageal pressure one may deduce the presence or absence of airway obstruction by simply measuring the speed with which air is expired This is easily done from a spirographic tracing which is a graphic record of the rate of

airflow from the lung during a forced expiration An index of airway caliber may be derived from this tracing in various ways Conventional indexes are the ratios of the volume of air expired in 1, 2, and 3 seconds to the total volume, or vital capacity Normal values exceed 70 85 and 97 per cent respectively An alternative method involves calculation of the rate of airflow during an arbitrary portion of the expirogram A convenient and reproducible measurement of this type is the maximal mid expiratory flow rate (M M F) which is the velocity of airflow in the middle half of a maximal expiration This may be easily calculated from the spirogram normal values exceeding 3 0 liters per second

LUNG STIFFNESS

The physical characteristics of any distensible structure including the lungs may be defined by measurement of the volume and of the pressure distending that structure at different levels of inflation If the relationship between pressure and volume is linear the compliance (volume/pressure) may be calculated The compliance is the degree to which the structure is distended by an increase of pressure

Lung compliance may be computed by measurement of the intrapulmonary pressure at various lung volumes Intraesophageal pressure may be used as a measure of intrapulmonary pressure and lung volume is measured by spirometry

REFERENCES

BRAUNWALD E *et al* The hemodynamics of the left side of the heart as studied by simultaneous left atrial left ventricular and aortic pressures particular reference to mitral to stenosis *Circulation 12* 69 1955

BRAUNWALD E TANENBAUM H L and MORROW A G Localization of *left to right cardiac shunts by dye-dilution curves following injection* into the left side of the heart and into the aorta *Am J Med 24* 203 1958

BROADBENT J C and WOOD E H Indicator dilution curves in acyanotic congenital heart disease *Circulation 9* 890 1954

DUBOIS A B BOTELHO S and COMROE J H JR A new method for *measuring airway resistance in man using a body plethysmograph* values in normal subjects and in patients with respiratory disease *J Clin Invest 35* 327 1956

GORLIN R and GORLIN S G Hydraulic formula for calculation of the area of the stenotic mitral valve other cardiac valves and central circulatory *shunts Am Heart J 41* 1 1951

KEYS J R SWAN H J C and WOOD E H Dye dilution curves from systemic arteries and left atrium of patients with valvular heart disease *Proc Staff Meet Mayo Clin 31* 138 1956

KORNER P I and SHILLINGFORD J P The quantitative estimation of valvular incompetence by dye dilution curves *Clin Sc 14* 553 1955

KORNER P I and SHILLINGFORD J P Further observations on the estimation of valvular incompetence from indicator-dilution curves *Clin Sc 15* 417 1956

McILROY M B and ELDRIDGE F L The measurement of the mechanical properties of the lungs by simplified methods *Clin Sc 15* 329 1956

MEAD J and WHITTENBERGER J L Physical properties of human lungs measured during spontaneous respiration *J Appl Physiol 5* 779 1953

MICHEL D HERBST M HARTLEB O and BLOCK K The diagnostic significance of the oxygen step in cardiac catheterization *Ztschr Kreislaufforsch 44* 902 1955

MORROW A G BRAUNWALD E HALLER J A and SHARP E H Left atrial pressure pulse in mitral valve disease A correlation of pressures obtained by transbronchial puncture with the valvular lesion *Circulation 16* 399 1957

SWAN H J C BURCHELL H B and WOOD E H Special applications of indicator-dilution technics in congenital and acquired heart disease *Proc Staff Meet Mayo Clin 31* 485 1957

CHAPTER 3

CONGENITAL HEART DISEASE

Physiological techniques for localization and quantitation of congenital structural anomalies of the heart were discussed in Chapter 2 In this chapter, the physiological consequences of left to-right and right to left shunts will be considered followed by a discussion of some specific congenital abnormalities The salient clinical features of each lesion will be mentioned and some physiological aspects of the diagnosis natural history and treatment will be discussed

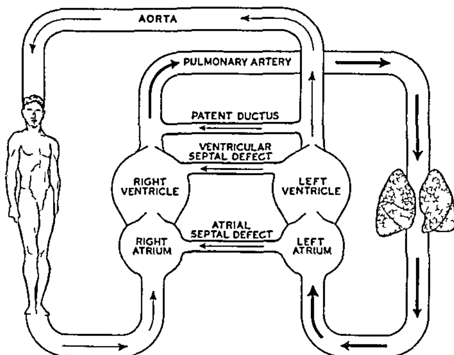
LEFT-TO RIGHT SHUNTS

Flow Load on Ventricles

Isolated communications between the left and right hearts are usually associated with left to right shunts The major effect of such a shunt is an increased flow load on one ventricle which must pump *the shunt flow in addition to the normal venous return* Figure 10 shows which ventricle bears the brunt of the load in the three common lesions In atrial defects the shunted blood flows from the left to the right atrium and is pumped forward by the right ventricle It returns to the left atrium and back to the right heart through the defect without ever being pumped by the left ventricle and so the flow load is borne entirely by the right ventricle In ventricular septal defect and in patent ductus arteriosus the left ventricle pumps the shunt flow into the pulmonary artery The shunted blood returns to the left atrium and is pumped around again through the lungs without ever being pumped by the right ventricle and thus all of the extra load is borne by the left ventricle This explains why right ventricular hypertrophy develops in atrial septal defect whereas left ventricular hypertrophy is usually present in the other lesions

Decreased Systemic Flow and Pulmonary Vascular Changes

In all three anomalies, excessive quantities of blood are pumped round and round through the lungs In addition to the extra flow load imposed on one ventricle, there may be accompanying decreased systemic flow and pulmonary vascular changes Decreased systemic flow is particularly apt to be present in atrial septal defects because



F g 10 S h mat c llustrat on of wh ch v tricl bears the b t of incr d flow in the th ee types of Intraca d ac l ft to right shunt I at ial s pt l defect th blood s sh ted f om the left to the r ght heart b fore t has been p mped by the left v t icle It is pumped to the lu g by the right ventricle which bea s the load of the extra flow In ventr cular def t and in p tent d ct s arte o us the l ft vent cle pumps the shunt flow d ctly to the l gs a d thus bears the load

so much of the venous return to the left side of the heart passes over to the right side of the heart instead of being pumped into the aorta This may lead to faulty growth and development

Excessive pulmonary blood flow may lead to pulmonary vascular changes with eventually pulmonary hypertension (see p 46)

RIGHT-TO LEFT SHUNTS

Normally, the pressure in the corresponding chamber of the right side of the heart is lower than that in the left so that flow is from the left to the right when there is a communication between the two sides However, pulmonic stenosis, tricuspid stenosis, or increased pulmonary vascular resistance can cause elevation of the pressure in the right side of the heart so that the flow is from right to left If the shunt is large, cyanosis results (Chap 11)

Flow Load on Ventricles

The effect of the right to left shunt on the heart is dependent upon the site of the shunt In Figure 11, a right to left shunt through a

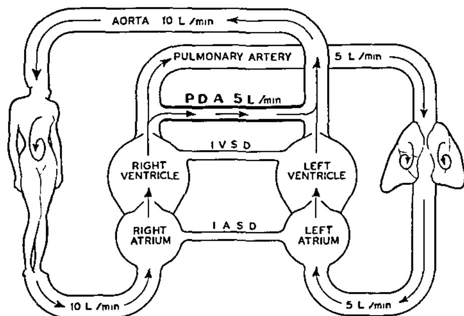


Fig 11 Schematic illustration of which ventricle bears the brunt of increased flow in various types of right to left shunt In atrial defect (I A S D) the shunted blood is pumped to the aorta by the left ventricle whereas in ventricular defect (I V S D) and in patent ductus arteriosus (P D A) the load is borne by the right ventricle

patent ductus arteriosus has been outlined and potential ventricular and atrial septal defects have also been shown In the case of the patent ductus arteriosus with reversed flow the right to left shunt consists of blood pumped from the right ventricle to the aorta The blood flow into and out of the right ventricle is excessive whereas the

left ventricular output is normal In this case the load is entirely upon the right ventricle A similar situation exists in a right to left shunt due to ventricular septal defect in which case the shunt flow is pumped by the right ventricle through the left ventricle into the aorta In the case of an atrial defect the flow load is on the left ventricle since the right to left shunt occurs before the blood has been pumped by the right ventricle

Systemic Hypoxia

In patients with a right to left shunt the oxygen supply to the tissues may be curtailed This is the result of the associated lesion responsible for the right to left direction of the shunt and is not due to the pres ence of the shunt itself In essence the amount of oxygen pumped to the tissues equals the amount of oxygen pumped from the lung into the aorta by the left ventricle If pulmonary blood flow is normal tissue oxygen supply is normal A right to left shunt causes additional unoxygenated blood to flow to the tissues This leads to reduction of the arterial oxygen saturation But the total systemic blood flow is increased so that tissue hypoxia is not present

Usually however a right to left shunt develops because of factors that also tend to reduce pulmonary blood flow and hence arterial hypoxemia is not associated with an adequate increase of total blood flow As a result the amount of oxygen brought to the tissues is re duced The first compensation for this is extraction of increased amounts of oxygen from the blood flowing through the tissues result ing in a decrease of the venous oxygen saturation The lower limit to which the resting venous oxygen tension can be reduced is about 30 mm Hg so that when the venous oxygen saturation falls to about 60 per cent the tissues are extracting a nearly maximal amount of oxygen from the blood

Polycythemia

At this point a second compensation appears increase of the circulating red blood cell mass This polycythemia increases the amount of oxygen that is carried by each volume of blood and so the amount of oxygen brought to the tissues by each unit of blood is increased

The management of the polycythemia associated with cyanotic congenital heart disease is a difficult problem The increased red cell

volume is apparently a result of stimulation of the bone marrow a direct or indirect result of hypoxemia, and results in an increased oxygen carrying power of the blood. This is desirable, from the stand point of tissue oxygenation, since a given unit of blood can carry almost twice as much oxygen when the hematocrit is 80 as it does at a hematocrit of 40 On the other hand, undesirable consequences result from the increased viscosity of the blood, which impedes circulation through the capillary networks This is particularly true in the lungs in which the vascular resistance is high, since the load on the right ventricle is increased and the right to left shunt is accentuated Although definitive principles have not been evolved for the management of this secondary polycythemia, one approach is to study each patient in terms of arterial oxygen saturation intracardiac pressures and blood flows in order to determine the level of hemoglobin concentration at which cardiopulmonary function is optimum and then to maintain that level by phlebotomy In the absence of such detailed studies, observations of the clinical course and of the arterial oxygen saturation may be adequate guides to therapy

INDIVIDUAL LESIONS

PULMONIC STENOSIS

Hemodynamic Abnormality

This lesion characterized by a murmur and thrill over the pulmonary valve, distant or absent pulmonic second sound (P2), and often poststenotic dilation of the pulmonary artery is amenable to surgical correction without resort to open heart surgery Although the lesion is not incompatible with a normal life span, symptoms of right heart failure generally appear before patients reach the age of 50 Right heart failure results from the fact that the narrow pulmonary valve imposes a strain on the right ventricle Since it is important to prevent this complication, and since symptoms often do not appear until relatively late in life an index of valve size is one factor which determines whether or not surgery is indicated As pointed out in Chapter 2 valve size is reflected in the magnitude of the pressure gradient across the pulmonic valve which, in turn is reflected in the height of the systolic pressure in the right ventricle In many clinics a right ventricular systolic pressure over 75 mm Hg is considered sufficient indication for surgical intervention Other indications in

clude right ventricular enlargement, evident on x ray or from electro cardiographic changes and symptoms of right ventricular failure

Surgical Treatment

Surgical repair of pulmonic stenosis may be accomplished by dilating the valve from below, through the ventricle, or by opening the pulmonary artery for visualization and incision of the valve under direct vision Preoperative and postoperative catheterization studies have shown that the latter is the method of choice and that pulmonic valvulotomy under direct vision is often followed by abolition of the pressure gradient across the pulmonary valve whereas the other procedure does not yield this favorable result

Infundibular Stenosis

The infundibular form of pulmonic stenosis is more difficult to repair surgically than is valvular stenosis and the distinction between the two types should be made preoperatively if possible The pulmonic second sound (P2) is more apt to be present in infundibular stenosis and poststenotic dilatation of the pulmonary artery may be absent This lesion is almost always associated with a ventricular septal defect Valvular stenosis may be accompanied by a diagnostic snapping sound early in systole possibly due to the jetlike ejection of blood into the pulmonary artery through the stenotic valve Catheterization and angiographic studies may help to define the nature of the lesion (Chap 2)

Valvular stenosis may be accompanied by some hypertrophy of the infundibulum which may regress slowly after surgical correction of the valvular lesion It is usually not necessary to correct this infundibular stenosis at the time of pulmonary valvulotomy Postoperative studies have revealed that the pressure gradient between the right ventricle and the pulmonary artery may not entirely disappear immediately after pulmonary valvulotomy but that it may gradually disappear during the ensuing months

Patent Foramen Ovale

Another common accompaniment of pulmonic stenosis is a patent foramen ovale This opening probe patent in 25 per cent of normal individuals may develop when right atrial hypertension the result of increased intraventricular pressure forces open the membranous flap

overlying the foramen ovale The anatomical location of this mem brane is such that it permits flow from the right to the left atrium but not from the left to the right atrium This results in a right to left shunt across the atrial septum with occasional cyanosis Since this

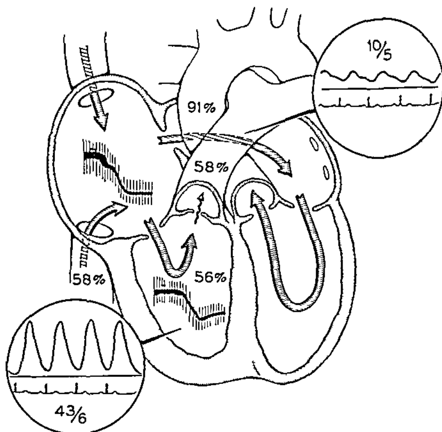


Fig 12 Intracard ac pressures oxygen saturat ons and dye curves obtained from the chambers of the right side of the heart in a patient with pulmonic stenosis and atrial septal defect Note (1) th h gh systol c p essu e (43 mm Hg) in the right ventricle and the low press e (10/5 mm Hg) n the p lmonary a te y beyond the stenotic p lmo c valve; (2) the double peaked dye curve f om the r ght at ium and the normal c rve from the ght t cle d ag ost c of a r ght to left shunt at the atr al le el; and (3) the sim lar o yg n sat rat on (56 to 58 per ce t) in all of the chambers of the r ght s de of the heart e cl d g a l lt to ght sh nt The red ced aort c (arterial) oxygen s t at on 91 p r c t i d e to the right to left shunt

defect may remain open after relief of the pulmonary stenosis it is best repaired at the time of surgery for the pulmonic stenosis and its presence should be ascertained preoperatively by physiological study Figure 12 is an example of the physiological abnormalities en

countered in a patient with pulmonic stenosis and patent foramen ovale

As mentioned in Chapter 2 atrial defects with a large left to right shunt may be associated with a pressure gradient across a relatively normal pulmonary valve or may lead to hypertrophy of the muscle in the right ventricular outflow tract resulting in infundibular stenosis This type of atrial defect must be distinguished from a patent foramen ovale complicating pulmonic stenosis Since the significant atrial shunt associated with severe pulmonic stenosis is from right to left a patient with a left to right shunt at the atrial level must be suspected of having secondary infundibular stenosis if a pressure gradient is measured between the right ventricle and the pulmonary artery In such a patient repair of the atrial defect should first be carried out and further surgical procedures should be based on the pressure reading in the right ventricle and pulmonary artery If open heart surgery is used for the primary repair surgical exploration of the pulmonary valve and infundibulum may be carried out without difficulty A preoperative angiocardiogram outlining the infundibulum and pulmonary valve may aid the surgeon in planning his operation

AORTIC STENOSIS

Diagnosis

This congenital lesion may be diagnosed by the presence of a murmur and thrill over the aortic area frequently transmitted to the neck absent aortic second sound (A2) and often dilatation of the aorta Confirmation of the diagnosis may be obtained by left heart catheterization or by angiocardiographic study

Surgical Treatment

Surgical experience with this lesion is considerably less than with pulmonic stenosis Although satisfactory opening of the aortic valve may be achieved with hypothermia and closed heart surgery open heart surgery with a pump oxygenator provides greater opportunity for definitive repair and is becoming increasingly the procedure of choice The congenital form of aortic stenosis is more easily repaired than the calcified valve found in the acquired form of the disease (Chap 5) At the present time patients with this defect are referred for surgery if they are subject to syncopal attacks possible precursors

to sudden death, or if they show evidence of left ventricular failure It is quite possible that with improvement of techniques this lesion will be corrected surgically upon making the diagnosis of a hemodynamically significant narrowing of the aortic valve since the ultimate prognosis is poor and since optimal therapeutic effect may best be achieved before the occurrence of calcification of the valve and/or irreversible left ventricular damage

ATRIAL SEPTAL DEFECT

Abnormal Hemodynamics

Characteristically atrial septal defect is associated with a large shunt from the left to the right atrium producing a load on the right ventricle The excessive pulmonary blood flow produces characteristic engorgement of the pulmonary vascular bed on x ray and a systolic murmur over the pulmonary valve

The reason for the left to right direction of the shunt is of interest At one time it was felt that blood flowed from left to right because the mean pressure is slightly higher in the left than in the right atrium However it has been found that the difference of mean pressure between the two atria is insufficient to account for the large shunt that exists and the current explanation is related to the fact that the left ventricle is less distensible than the right For a given degree of filling, the pressure in the left ventricle rises higher than it does in the right As a result it is easier for blood to flow into the right than into the left ventricle The higher pressure in the left atrium at the end of diastole rather than the higher mean left atrial pressure is responsible for the left to right direction of the shunt

Since the shunt in atrial defect is from left to right subnormal amounts of blood enter the left ventricle and left ventricular output is reduced Diminished systemic blood flow may result in faulty development and in fatigue a common complaint in this condition Eventually the overloaded right ventricle may fail with characteristic signs and symptoms

Pulmonary Hypertension

As in any large left to right shunt with excessive pulmonary blood flow, obstructive changes may occur in the pulmonary vascular bed The frequent respiratory infections which occur in these patients may be a factor in the development of pulmonary vascular changes In

patients with atrial defects these changes usually do not occur until after the age of twenty The mild pulmonary hypertension seen in children with this lesion may be ascribed to the excessive pulmonary blood flow Later in life severe elevation of the pulmonary artery pressure may result from the increased pulmonary vascular resistance and may further promote the development of failure of the right ventricle This causes a rise of right atrial pressure and a reversal of the direction of flow through the atrial defect with resultant cyanosis At this point, the atrial defect becomes a protective mechanism to prevent overloading of the right ventricle and closure may result in acute right ventricular failure It is important to make the diagnosis of atrial septal defect early in life and to institute definitive surgery as soon as practical when the volume of flow through the defect is large or when the pressure in the pulmonary artery begins to rise Since the pulmonary vascular changes secondary to this lesion may be largely irreversible surgery should be done before they develop Some individuals consider that the mere presence of an atrial defect as in the case of a patent ductus arteriosus is sufficient indication for surgery

Rarely for reasons as yet unknown the shunt through an atrial defect may be from right to left in the absence of pulmonary vascular changes or indeed of right ventricular hypertension Such a defect may probably be closed without hazard

The diagnosis of a shunt at the atrial level depends upon the methods outlined in Chapter 2 Passage of a cardiac catheter through an atrial defect is best accomplished from below so that catheterization via a saphenous or femoral rather than a basilic vein is more apt to lead to successful appreciation of the site of the defect If the catheter does not pass through the defect a left to right shunt can be diagnosed by the presence of an oxygen step-up at the atrial level or by indicator-dilution curves after inhalation of the indicator or after injection of the indicator into the left atrium A right to-left shunt is detected by dye dilution curves (Chap 2) The presence of a pressure gradient across the pulmonic valve in some patients with uncomplicated atrial defect has been discussed above (Pulmonic Stenosis)

The Valsalva maneuver with oximetric measurement of the arterial oxygen saturation may be a helpful diagnostic measure During the performance of the Valsalva maneuver the blood is dammed in back of the right atrium because of the rise of intrathoracic pressure Upon release of the forced expiration or strain this blood flows into the

right atrium causing the pressure therein to rise briefly to a level higher than that in the left atrium As a result, the blood flows from right to left through the atrial defect and there is a temporary fall of the arterial oxygen saturation Such a fall of oxygen saturation is not seen in normal subjects after release of a forced expiration and may be diagnostic of an atrial defect

Atrioventricularis Communis

Most atrial septal defects are of the ostium secundum type high in the septum and can be repaired without the use of cardiac bypass The rarer primum defect frequently involves the mitral valve and upper ventricular septem atrioventricularis communis This lesion is often associated with mitral valve insufficiency and ventricular septal defect It is difficult to repair and requires open heart surgery It is very common in mongolism and should be suspected in the presence of a systolic murmur to the left of the sternum or over the apex left ventricular hypertrophy by x ray or electrocardiogram, and severe pulmonary hypertension which is often present Diagnosis may be confirmed (1) by the passage of a cardiac catheter through a low lying septal defect (2) by dye dilution studies after injection of dye into each pulmonary artery (3) by the demonstration by dye injection into the left ventricle of the accompanying mitral insufficiency and (4) by the presence of a second oxygen step up at the ventricular level

Anomalous Pulmonary Venous Return

A condition which may be indistinguishable clinically and physiologically from an atrial defect is anomalous pulmonary venous return One or all of the pulmonary veins may drain into the right atrium and the left to right shunt at the atrial level results in a similar murmur in the pulmonic area and engorged pulmonary vessels like those found in atrial defect Catheterization findings are also similar unless a careful search is made for the orifices of the veins Differential diagnosis may be made by passage of a catheter directly into the aberrant vein(s) from the right atrium but it may be difficult to be certain whether or not the catheter first passed through an atrial defect into the left atrium and then into a pulmonary vein Dye dilution curves are useful in making this distinction If the dye-dilution curve recorded after injection of dye into a pulmonary vein is similar

to that seen after injection of dye into the superior vena cava anomalous venous return is very likely to be present In most atrial defects a different curve will be obtained because much of the dye injected into the pulmonary vein enters the left atrium and continues on to appear in the systemic circulation Anomalous venous return is frequently accompanied by an atrial defect, and the surgical repair of one defect should include thorough exploration for the other

VENTRICULAR SEPTAL DEFECT

Abnormal Hemodynamics

This common anomaly is characterized by a loud murmur and thrill maximal over the lower left sternum It may be small and of no consequence to the patient Indeed a small defect may result in the production of a loud murmur and yet the amount of flow through it may be insufficient to cause enough alteration of the oxygen saturation of the right ventricular blood so as to be detectable by cardiac catheterization Larger defects however produce a step up of oxygen saturation at the ventricular level which is diagnostic

The magnitude and direction of the flow through a ventricular defect depend upon the size and configuration of the defect and upon the pressure in each ventricle Normally the pulmonary vascular resistance is much less than the systemic vascular resistance and so the systolic pressure in the right ventricle is much lower than that in the left ventricle Thus the flow through the defect is from left to right and the amount of shunt is dependent upon the size of the defect The hemodynamics are similar to those encountered in atrial defect except that the flow load is on the left rather than on the right ventricle As a result left ventricular hypertrophy may be apparent on x ray and/or the electrocardiogram Although the pulmonary blood flow is increased by the left to right shunt the systemic flow is not apt to be reduced as much as it is in atrial septal defect and hence faulty growth and development are less common findings

Pulmonary Hypertension

As in atrial septal defect pulmonary vascular changes and increased pulmonary vascular resistance may lead to increased pulmonary artery pressure with reversal of the direction of the shunt Pulmonary hypertension may be present in these patients from birth or it may develop later in the course of the patient s life

FROM BIRTH In the fetus, the pulmonary vascular resistance is much greater than it is in a child or adult As a result, the small amount of blood flowing to the lung causes a high pressure in the pulmonary artery This pressure is higher than the aortic pressure with the consequence that oxygenated blood returning to the heart from the placenta, cannot enter the lung through the ductus arteriosus At birth, as the lungs inflate and the vessels are thereby opened, the pulmonary vascular resistance falls immediately It continues to diminish slowly as the medial hypertrophy characteristic of the fetal arterioles is replaced by the thinner walled vessels of the adult type In infants with a large ventricular defect the pulmonary vasculature may retain the fetal characteristics the pulmonary artery pressure then remains high This may be considered to be a protective mechanism that prevents most of the left ventricular output from going to the lung instead of to the systemic tissues Thus the presence of increased pulmonary vascular resistance and hence of pulmonary hypertension may be a life saving adaptation for infants with a large ventricular septal defect

LATE Severe pulmonary hypertension may also develop as a secondary complication of ventricular septal defect It is apt to develop at an earlier age than it does in atrial defects It only occurs in relatively large defects and if so there is usually some pulmonary hypertension from birth

Surgical Treatment

Patients with a small ventricular septal defect without pulmonary hypertension may never develop complications and so are not considered candidates for surgery at present They should be carefully observed and possibly catheterized periodically in order to detect pulmonary hypertension if it develops but before it becomes so severe that surgery cannot be performed

Patients with mild pulmonary hypertension are apt to develop increasing elevation of the pulmonary artery pressure with the passage of time so that particularly if the left to right shunt is large they are now considered ideal candidates for surgery

When pulmonary hypertension is severe either in infancy or as a later development and the shunt is from right to left surgery is extremely hazardous and probably not indicated Under these condi

tions, the limiting factor is the restricted pulmonary vascular bed and surgical repair of the ventricular defect does nothing to improve the pulmonary circulation Some infants with severe pulmonary hypertension associated with a ventricular septal defect have been found to improve on conservative treatment and to reveal decreased pulmonary artery pressure with the passage of time

PULMONARY VASOCONSTRICTION Some of the pulmonary hypertension seen in patients with ventricular defects may be due to pulmonary vasoconstriction if that is the case surgical repair is less hazardous than if all of the increased pulmonary vascular resistance is due to anatomical changes in the blood vessels One technique for selecting such patients for surgery is to study the pulmonary artery pressure before and after oxygen breathing Reversible pulmonary hypertension is characterized by reduction of the pressure in the pulmonary artery or of the right to left shunt after oxygen breathing whereas irreversible pulmonary hypertension is unaffected Drugs such as acetylcholine may exert a similar effect on the pulmonary circulation and thus prove to be of prognostic value

Infundibular Stenosis

As in atrial septal defects excessive flow from the left ventricle through a ventricular defect may lead to infundibular stenosis This raises the pressure in the right ventricle leading eventually to a right to left shunt Since repair of ventricular defects requires open heart surgery an associated infundibular lesion can also be repaired Right ventricular hypertension if due to infundibular stenosis is not a contraindication to surgery The critical factor in selecting these patients for surgery is the level of the pressure in the pulmonary artery and not the pressure in the right ventricle A high right ventricular pressure is not necessarily a contraindication to surgery whereas severe pulmonary hypertension is

PULMONIC STENOSIS AND VENTRICULAR SEPTAL DEFECT (TETRALOGY OF FALLOT)

Abnormal Hemodynamics

The common association of pulmonic stenosis and ventricular septal defect may be partially ascribed to the fact that infundibular stenosis may be a consequence of a large ventricular defect (see

above) In most cases, however, both lesions develop in the embryo Because of the pulmonic stenosis, right ventricular hypertrophy is present The ventricular defect is usually so high that the aorta appears to override the right ventricle The combination of pulmonic stenosis, ventricular septal defect right ventricular hypertrophy and overriding of the aorta is called the tetralogy of Fallot

Actually the pulmonic stenosis and the ventricular septal defect are the two important lesions and the severity of each determines the pathophysiology and the clinical picture Most commonly, a moderate ventricular defect is accompanied by a moderate to severe pulmonic stenosis so that the pressure is the same in the two ventricles and there is some right to left shunt This results in cyanosis and the classic picture of the tetralogy of Fallot However marked pulmonic stenosis may occur in the presence of a small ventricular defect with the result that the shunt is small and the cyanosis minimal This lesion is similar clinically and physiologically to isolated pulmonary stenosis (see above) Finally, a large ventricular defect may be associated with mild pulmonary stenosis in which case the shunt is from left to right and the picture is essentially, that of a ventricular septal defect (see above)

Patients with a moderate defect and fairly severe pulmonary stenosis present a characteristic picture of cyanosis since birth typical boot shaped heart on x ray due to the small pulmonary artery and the right ventricular hypertrophy and a precordial systolic murmur with delayed or absent pulmonic second sound Attacks of loss of consciousness and deepening cyanosis are common in these patients They are accompanied by a decrease or absence of the systolic murmur and a sharp increase of the right to left shunt This is not due to systemic vasodilatation because the systemic blood pressure remains normal The pressure in the pulmonary artery has been found to fall sharply This combination of findings is best explained by a transient increase of the degree of infundibular stenosis though pulmonary arteriolar vasoconstriction and systemic vasodilatation may be factors which contribute to the increased right to left shunt

Surgical Treatment

Until recently the surgical approach to this problem has been to increase the pulmonary circulation by creation of an artificial

ductus arteriosus (Blalock operation) or by direct anastomosis of the aorta to the pulmonary artery (Potts operation) These operations increase the blood flow to the lung with two opposite effects on tissue oxygen supply More oxygenated blood returns to the left ventricle which tends to increase the arterial oxygen saturation On the other hand, the systemic flow may be diminished because of the left to right shunt so that the amount of oxygen brought to the tissues may be reduced An interesting theoretical analysis by Otis revealed that the optimal oxygen supply to the tissues would be achieved in a patient with no pulmonary blood flow to start with if a 50 per cent shunt were created Larger or smaller shunts would result in less oxygen supply to the tissues These procedures, though not curative have resulted in improvement of large numbers of children having the tetralogy of Fallot but they are being replaced by more definitive surgical correction of the existing lesions

In a number of patients, surgical relief of pulmonary stenosis alone has been followed by sudden death This may be ascribed to sudden reversal of the direction of the shunt through the ventricular septum with abrupt diminution of the systemic blood flow due to the inability of the left ventricle to handle the increased flow Some degree of pulmonic stenosis may be necessary for maintenance of systemic flow in these patients just as preservation of the fetal architecture in the pulmonary circulation is necessary for survival of some infants born with a large ventricular defect Surgical correction of the pulmonic stenosis should be accompanied by correction of the ventricular defect If such open heart surgery is contraindicated the patient should have a Blalock or Potts operation or if possible be managed medically until definitive surgery is possible

PATENT DUCTUS ARTERIOSUS

Abnormal Hemodynamics

This surgically curable lesion generally does not require investigation by catheterization or angiography to establish the diagnosis In most instances it can be recognized by the characteristic machinery murmur over the first to second left interspace Diagnosis may be made by the use of dye curves or by the finding of an oxygen step up in the pulmonary artery at cardiac catheterization An aortico pulmonary defect may produce nearly identical clinical and physiological findings The differential diagnosis may be made with

certainty only by angiocardiography or by passing a catheter through the defect so that the location of the communication can be visualized In view of the possible development of complications and of the ease of definitive cure, surgical treatment is indicated in every uncomplicated case

Pulmonary Hypertension

One serious complication is the development of pulmonary hypertension Usually this is a late development but it may as in ventricular defect, be present in infancy It leads to reversal of the direction of the blood flow through the ductus The resultant cyanosis is more severe in the lower than in the upper extremity because of the site of entrance of the ductus into the aorta In addition, the machinery murmur may be replaced by only a systolic or diastolic murmur or rarely by no murmur at all Surgical correction of such a lesion is fraught with hazards although it has been carried out One approach involves temporary occlusion of the ductus preferably with pressure measurements in the right ventricle to determine whether or not permanent occlusion could be tolerated As in ventricular septal defect vasoconstriction may play a part in the genesis of the pulmonary hypertension in which case surgical repair is probably less hazardous

COARCTATION OF THE AORTA

This lesion must be excluded in every patient with hypertension by measurement of the blood pressure in the legs It is another lesion whose presence warrants surgical correction Angiographic studies may be helpful to the surgeon in providing preoperative outline of the lesion but physiological studies except for intra arterial pressure measurements, are of little help in diagnosis or evaluation

At operation the effectiveness of the surgery may be evaluated by direct pressure readings above and below the anastomosis or graft If a significant gradient persists further surgery may be indicated The systemic hypertension in these patients is presumably due to renal ischemia for the blood pressure frequently does not fall immediately after surgery Usually, a successful operation is followed by a gradual fall of blood pressure and the presence of hypertension in the immediate postoperative period does not mean that surgery was inadequate

EBSTEIN S ANOMALY OF THE TRICUSPID VALVE

Abnormal Hemodynamics

In this serious form of congenital heart disease the abnormal tricuspid valve is misplaced forward into the right ventricle and is incompetent The right ventricular cavity is very small and the right atrium is greatly enlarged There is usually an associated atrial septal defect Because of the tricuspid insufficiency and right ventricular inadequacy the right atrial pressure is elevated and the shunt through the atrial defect tends to be from right to left producing mild cyanosis Additional findings are bizarre variable systolic and diastolic murmurs usually to the left of the lower sternum right bundle branch block on the electrocardiogram and relatively normal physical development Serious arrhythmias are common and are probably responsible for the very poor prognosis

Diagnosis

The diagnosis may be made at cardiac catheterization by visualiza tion of the catheter in the huge right atrium passing through the misplaced tricuspid valve Intracavitary electrocardiography is par ticularly helpful in this lesion The atrial wall just proximal to the tricuspid valve where ventricle is normally present consists of some ventricular muscle The intracavitary electrocardiogram at this site is of a ventricular type rather than atrial in nature whereas an atrial rather than a ventricular pressure pulse is present This finding of an atrial pulse in the presence of an intracavitary ventricular elec trocardiogram has been considered diagnostic

Surgical correction of this lesion is not satisfactory but a shunt from the superior vena cava to the right pulmonary artery as per formed by W W L Glenn might be beneficial Since cardiac catheterization has resulted in sudden death from arrhythmias there is some question as to whether or not catheterization should be per formed in individuals suspected of having this lesion However many patients have been safely catheterized If the electrocardiogram is carefully monitored and the procedure terminated abruptly upon the appearance of an arrhythmia the risk is not too great

TRICUSPID ATRESIA

Complete obliteration of the tricuspid valve must be suspected in cyanotic infants with left ventricular hypertrophy In these patients

blood passes from the right to the left atrium through an atrial defect, and pulmonary circulation is maintained through a ventricular defect or a patent ductus arteriosus The right ventricle is hypoplastic and circulation is maintained almost entirely by the left ventricle Cyanosis is inevitable, and life depends upon the adequacy of the pulmonary blood flow

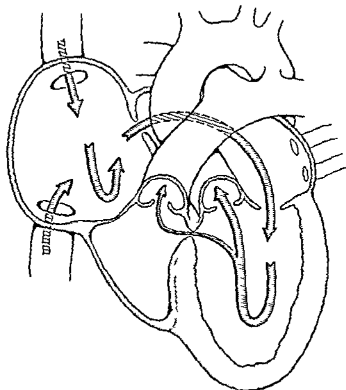


Fig 13 Tricuspid atresia with atrial and ventricular defects A patent ductus arteriosus had probably closed just before death Blood entering the right artium passed through the atrial defect to enter the left ventricle Some of this blood mixed with pulmonary venous blood reached the pulmonary artery via the ventricular septal defect

The patient illustrated in Figure 13 had a patent ductus arteriosus in addition to the defects mentioned above At autopsy the ductus arteriosus was found to be practically closed Presumably adequate circulation to the lungs was dependent upon flow through the ductus in addition to that through the ventricular defect When the ductus closed, life could not be maintained In the absence of more definitive

surgery a Blalock or Potts operation might improve such a patient but the prognosis is generally very poor

TRANSPOSITION OF THE GREAT VESSELS

In this lesion the aorta arises from the right ventricle and the pulmonary artery from the left ventricle Each ventricle pumps blood back to itself Life depends upon the coexistence of a communication between the two sides of the heart This may be an atrial defect, a ventricular defect a patent ductus arteriosus or a combination of these The diagnosis is generally obvious clinically from severe cyanosis cardiac enlargement and evidence of increased pulmonary blood flow Definitive diagnosis may be made by angiocardiography or by cardiac catheterization if all of the cardiac chambers are entered The prognosis is very poor, but there is hope that improving techniques of open heart surgery will eventually permit operative cure

Taussig Bing Syndrome

A less ominous form of this lesion incomplete transposition or the Taussig Bing syndrome consists of partial transposition of the pulmonary artery complete transposition of the aorta and a high ventricular septal defect In this lesion more of the oxygenated blood returning from the lungs is pumped by the left ventricle into the pulmonary artery than into the aorta so that the oxygen saturation is higher in the pulmonary artery than in the aorta just as it is in complete transposition This fact, plus cyanosis from birth distinguishes the syndrome from ventricular septal defect with pulmonary hypertension and a right to left shunt which it may resemble clinically

REFERENCES

GENERAL

BAHNSON H T and OTIS A B Physiological considerations of cardiovascular surgery *Physiol Rev* *35* 363 1955

BING R. J Congenital heart disease An introduction and classification *Am J Med* *12* 77 1952

BROTMACHER L and DEUCHAR D C The systemic blood flow in congenital heart disease with an examination of the validity of the cardiac index *Clin Sc* *15* 441 1956

DAMMANN J F JR and FERENCZ, C The significance of the pulmonary vascular bed in congenital heart disease III Defects between the ventricles or great vessels in which both increased pressure and blood flow may act upon the lungs and in which there is a common ejectile force *Am Heart J* *52* 210 1956

DAVISON P H ARMITAGE G H and ARNOTT W M The mechanisms of adaptation to a central venous arterial shunt *Brit Heart J* *15* 221 1953

EDWARDS J E Functional pathology of the pulmonary vascular tree in congenital cardiac disease *Circulation* *15* 164 1957

FERENCZ C and DAMMANN J F Significance of the pulmonary vascular bed in congenital heart disease V lesions of the left side of the heart causing obstruction of the pulmonary venous return *Circulation* *16* 1046 1957

HOLLING H E Compensatory mechanisms for the anoxia of cyanotic congenital heart disease *Clin Sc* *11* 282 1952

KJELLBERG S R MANNHEIMER E RUDHE U and JONSSON B *Diagnosis of Congenital Heart Disease* Chicago Year Book Publishers 1955

MACMAHON B MCKEOWN T and RECORD R G The incidence and life expectation of children with congenital heart disease *Brit Heart J* *15* 121 1953

SWAN H J C ZAPATA DIAZ J BURCHELL H B and WOOD E H Pulmonary hypertension in congenital heart disease *Am J Med* *16* 12 1954

WOOD P *Diseases of the Heart and Circulation* Philadelphia Lippincott 1956

PULMONARY STENOSIS AND TETRALOGY OF FALLOT

BLOUNT S G JR VAN ELK J BALCHUM O J and SWAN H Valvular pulmonary stenosis with intact ventricular septum clinical and physiologic response to open valvuloplasty *Circulation* *15* 814 1957

CALLAHAN J A BRANDENBURG R O and SWAN H J C Pulmonary stenosis and interatrial communication with cyanosis Hemodynamic and clinical study of ten patients *Am J Med* *19* 189 1955

CAMPBELL M Simple pulmonary stenosis pulmonary valvular stenosis with closed ventricular septum *Brit Heart J* *16* 273 1954

ENGE M A HOLSWADE G R GOLDBERG H P LUKAS D S and GLENN F Regression after open valvotomy of infundibular stenosis accompanying severe valvular pulmonic stenosis *Circulation* *17* 862 1958

MCCORD M C VAN ELK JR. and BLOUNT S G JR Tetralogy of Fallot Clinical and hemodynamic spectrum of combined pulmonary stenosis and ventricular septal defect *Circulation* *16* 736 1957

SHEPARD R J Redistribution of systemic blood flow in pulmonary stenosis *Brit Heart J* *17* 98 1955

SILVERMAN B K NADAS A S WITTENBORG M H GOODALE W T and GROSS R E Pulmonary stenosis with intact ventricular septum Correlation of clinical and physiologic data with review of operative results *Am J Med* *20* 53 1956

SEPTAL DEFECTS

BAHNSON H T and WILLIAMS G R Physiologic considerations of intra cardiac pressures following closure of atrial septal defects *J Thoracic Surg 34* 685 1957

BLOUNT S G JR BALCHUM O J and GENSINI G The persistent ostium primum atrial septal defect *Circulation 13* 499 1956

BLOUNT S G JR SWAN H GENSINI G and McCORD M C Atrial septal defect Clinical and physiologic response to complete closure in five pa tients *Circulation 9* 801 1954

BROTMACHER L and CAMPBELL M The natural history of ventricular septal defect *Brit Heart J 20* 97 1958

DEXTER L Atrial septal defect *Brit Heart J 18* 209 1956

KIRKLIN J W WEIDMAN W H BURROUGHS J T BURCHELL H B and WOOD E H Hemodynamic results of surgical correction of atrial septal defect a report of 33 cases *Circulation 13* 825 1956

MANHEIMER W IKKOS D and JONSSON B Prognosis of isolated ventricular septal defects *Brit Heart J 19* 333 1957

SCEBAT L VORIDIS E RENAIS J et LENÈGRE J L hypertension arterielle pulmonaire dans les communications interauriculaires interventriculaires et aorto pulmonaires *Arch mal cœur 50* 801 1957

SCEBAT L VORIDIS E RENAIS J et LENÈGRE J Étude du mécanisme des shunts dans les communications interauriculaires interventriculaires et aorto-pulmonaires *Arch mal cœur 50* 818 1957

SEPULVEDA G LUKAS D S and STEINBERG I Anomalous drainage of pul monary veins clinical physiologic and angiocardiographic features *Am J Med 18* 883 1955

SWAN H J C TOSCANO-BARBOZA E and WOOD E H Hemodynamic find ings in total anomalous pulmonary venous drainage *Proc Staff Meet Mayo Clin 31* 177 1956

SWAN H J C KIRKLIN J W BECU L M and WOOD E H Anomalous connection of right pulmonary veins to superior vena cava with interatrial communications hemodynamic data in eight cases *Circulation 16* 54 1957

WAKAI C S and EDWARDS J E Development and pathologic considerations in persistent common atrioventricular cenal *Proc Staff Meet Mayo Clin 31* 487 1956

WAKAI C S SWAN H J C and WOOD E H Hemodynamic data and find ings of diagnostic value in nine proved cases of persistent common atrioven tricular canal *Proc Staff Meet Mayo Clin 31* 500 1956

WOOD P MAGIDSON O and WILSON P A O Ventricular septal defect with note on acyanotic Fallot s tetralogy *Brit Heart J 16* 387 1954

PATENT DUCTUS ARTERIOSUS

COSH J A Patent ductus arteriosus *Brit Heart J 19* 13 1957

ELLIS F H KIRKLIN J W CALLAHAN J A and WOOD E H Patent duc

tus arteriosus with pulmonary hypertension An analysis of cases treated surgically *J Thoracic Surg 31* 268 1956

FOWLER N O and MANNIX E P Estimation of the size of the patent ductus arteriosus from hemodynamic data. *J Clin Invest 34* 1242 1955

COARCTATION OF THE AORTA

CAMPBELL M and BAYLIS J H The course and prognosis of coarctation of the aorta *Brit Heart J 18* 475 1956

COUNIHAN T B Changes in the blood pressure following resection of coarctation of the aortic arch *Clin Sc 15* 149 1957

WRIGHT, J L BURCHELL H B WOOD E H HINES E A JR and CLAGETT O T Hemodynamic and clinical appraisal of coarctation four to seven years after resection and end to end anastomosis of the aorta *Circulation 14* 806 1956

EBSTEIN S ANOMALY OF THE TRICUSPID VALVE

BLOUNT S G JR McCORD M C and GELB I J Ebstein s anomaly *Circulation 15* 210 1957

HERNANDEZ, F A ROCHKIND R and COOPER H R The intracavitary electrocardiogram in the diagnosis of Ebstein s anomaly *Am J Cardiol 1* 181 1958

MAYER F E NADAS A. S and ONGLEY P A Ebstein s anomaly presentation of ten cases *Circulation 16* 1057 1957

YIM B J B, and YU P N Value of an electrode catheter in diagnosis of Ebstein s disease *Circulation 17* 543 1958

TRICUSPID ATRESIA

BROWN J W HEATH D MORRIS T L and WHITAKER W Tricuspid atresia. *Brit Heart J 18* 499 1956

TRANSPOSITION OF THE GREAT VESSELS

CHIECHI M Incomplete transposition of the great vessels with biventricular origin of the pulmonary artery (Taussig Bing complex) Report of four cases and review of the literature *Am J Med 22* 234 1957

CHAPTER 4

HEART FAILURE

Heart failure may be defined as failure of the heart to pump adequate quantities of blood to meet tissue requirements for oxygen It may be present at rest or, in milder cases only during exercise It may be the result of impaired myocardial function of an overwhelm ing load imposed upon a normal myocardium, or as in hemorrhagic shock of reduction of the circulating blood volume so that central venous pressures are so low that the cardiac output is reduced The underlying cause of heart failure may be a sudden, overwhelming event—acute heart failure—or it may be milder and of more gradual onset—chronic heart failure The nature of the symptoms signs and physiological abnormalities present in the patient with heart failure depends upon all of these factors and upon the location of the under lying abnormality

MYOCARDIAL FUNCTION

Heart failure is not synonymous with myocardial failure Heart failure means that the over all pumping action of the heart is made quate to meet tissue demands for oxygen whereas myocardial failure means that the heart is not contracting with normal force under given conditions Thus very heavy exercise in a normal person even an athlete is associated with heart failure in that the heart is pumping insufficient blood to the exercising limbs Yet the myocardium is re sponding normally to the stimuli which cause it to contract In mitral stenosis the cardiac output is often inadequate despite normal myo cardial function (Chap 5) The fault lies in the obstruction to the flow of blood through the mitral valve

In order to assess myocardial function and its relationship to heart failure it is necessary to review normal myocardial function and the criteria of its abnormality

Ventricular Function Curves

A convenient framework in which to discuss this subject is offered by Sarnoff's modification of the Starling relationship between myocardial work and end diastolic fiber length of the ventricle As observed in the isolated heart the force of myocardial contraction or stroke work depends upon the length of the muscle fiber at the onset of the contraction (Chap 1) After a certain point however, stretching of the muscle results in a decrease rather than an increase of the forcefulness of contraction (the descending limb of Starling's curve) The degree of stretch of the myocardial fiber is reflected in

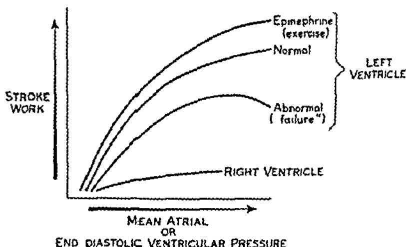


Fig 14 Schematic ventricular function curves for normal right ventricles and for left ventricle when normal when stimulated by epinephrine as during muscular exercise and when abnormal as in myocardial failure Note that the descending limb appears only on the abnormal ventricular function curve (Modified from the experimental work of S J Sarnoff and associates)

the size of the ventricle at the end of diastole This in turn is reflected by the height of the end-diastolic pressure which is reflected in the level of the atrial pressure Thus myocardial function may be assessed by measuring the stroke work at various levels of atrial pressure

Sarnoff has studied the relationship between stroke work and atrial pressure under a variety of conditions in dogs and has developed the concept of a family of ventricular function curves As plotted in Figure 14 the function of the ventricle may be described as a curve relating stroke work to atrial pressure Increased pressure causes an

creased work and there is a normal level of work for each atrial pressure Under the influence of drugs or of humoral or nervous stimulation the relationship between work and pressure may change Apparently there is no descending limb on the ventricular function curve of the normal intact heart

The failing myocardium performs a subnormal amount of stroke work for each filling pressure In addition an increase of filling pressure eventually causes decreased stroke work (the descending limb) These two features of the ventricular function curve distinguish the failing from the normal myocardium

Stroke work is affected both by change of ventricular function and by change of filling pressure The normal myocardium responds to increased filling with an increase of stroke work whereas the failing myocardium may respond to increased filling with a decrease of stroke work That is why reduction of the venous pressure, by phlebotomy or by the application of tourniquets may result in an increase of stroke work and of cardiac output in individuals with myocardial failure but not in normals

TYPES OF HEART FAILURE

Reduced Blood Volume

Hemorrhage and systemic vasodilatation lead to reduction of the venous pressure in both the lesser and the greater circulations This causes decreased filling of the ventricles during diastole As a result the length of the myocardial fibers at the end of diastole is subnormal the ventricle beats with less force and cardiac output falls Reflex tachycardia may cause some increase of cardiac output but this may be inadequate to meet tissue requirements if the central venous pressures are very low In this situation heart failure is present despite normal myocardial function Therapy is directed at replacing lost blood volume or at restoring normal vascular tone Chronic anemia which may be associated with abnormal myocardial function because of myocardial hypoxia is discussed in Chapter 5 (Hyperkinetic States)

Obstruction to Ventricular Outflow

The sequence of events which follows obstruction to ventricular outflow is similar for both sides of the heart Faced with a sudden

increase in resistance to outflow, the ventricle ejects a subnormal stroke volume Since the stroke work is predetermined by the length of the myocardial fibers at the end of the previous diastole stroke volume must fall when resistance to outflow is increased Since systolic emptying is incomplete, the volume of blood in the ventricle at the beginning of the next diastole is increased Normal diastolic filling results in an increased amount of blood in the ventricle at the end of diastole This in turn causes an increased end diastolic fiber length

TABLE 1 HEART FAILURE

General cause	Specific cause	
	Acute	Chronic
Reduced effective blood and/or red cell volume	Hemorrhage Neurogenic shock	Anemia
Obstruction to ventricular outflow	Pulmonary emboli	Occlusive pulmonary vascular disease pulmonary fibrosis emphysema pulmonic stenosis
	Hypertensive crisis	Aortic stenosis hypertensive cardiovascular disease coarctation of aorta
Increased flow requirement	Valvular insufficiency Arteriovenous fistula	Valvular insufficiency arteriovenous fistula septal defects beriberi anemia thyrotoxicosis
Obstruction to ventricular inflow	Atrial tumor	Mitral or tricuspid stenosis constrictive pericarditis vena caval obstruction
Myocardial weakness	Ischemic heart disease Myocarditis	Ischemic heart disease myocarditis myocardial fibrosis

and the next beat is more forceful Blood flow may now be maintained at a normal level but at a slightly higher end diastolic and mean atrial pressure Further increase of resistance to ventricular outflow causes further elevation of atrial and venous pressure This may lead in the case of the left heart to pulmonary congestion and pulmonary edema Elevation of the right atrial and systemic venous pressures occurs in pulmonary hypertension Myocardial failure may not be present in either case since ventricular function may be normal However inspection of the normal ventricular function curve

reveals that a very small increase of pressure results in a large in crease of stroke work so that a large increase of stroke work may occur with little elevation of venous pressure

Acute obstruction to ventricular outflow can be produced experi mentally and follows massive pulmonary embolism in patients It is associated with marked elevation of intraventricular systolic pressure If more than three fourths of the cross sectional area of the aorta or of the pulmonary artery is obstructed dilation of the heart ineffectual beats and eventually cardiac standstill result This type of acute myocardial failure may be partially due to myocardial ischemia re sulting from increased myocardial work in the face of a reduced cardiac output

Sustained chronic obstruction to ventricular outflow occurs in aortic stenosis in pulmonic stenosis and in systemic and pulmonary hypertension In each case, the increased stroke work is accompanied by increased end diastolic pressure in the ventricle and increased atrial pressure Whether or not the latter may become so high as to cause systemic or pulmonary edema when ventricular function is still normal cannot be answered at this time The studies that have been done suggest that cardiac dilatation and venous hypertension are as sociated with abnormal myocardial function

Sustained stress causes myocardial hypertrophy The extent to which this is beneficial in terms of ventricular function remains to be ascertained Presumably a hypertrophied heart if adequately per fused with blood can generate more power with each beat at a given level of stretch Its ventricular function is supernormal But such a myocardium may be more disposed to fail because of the excessive requirements for blood flow

Increased Flow Requirements

As in obstruction to ventricular outflow the increased myocardial work required to maintain an elevated flow is achieved by increased end diastolic pressure For example immediately after the onset of mitral insufficiency part of the left ventricular stroke volume regurgi tates into the left atrium The forward stroke output is correspond ingly reduced and the left atrial pressure is elevated The latter causes increased filling of the ventricle during the next diastole so that the next stroke volume is increased This continues until forward flow becomes normal A similar adjustment occurs in aortic insuffi

ciency, except that ventricular end diastolic volume is elevated by blood flowing back from the aorta rather than forward from the atrium

Stress of this type leads to increased stroke work and volume though forward flow is normal or reduced with elevated end diastolic and atrial pressures Again as in obstruction to outflow a small rise of pressure may be associated with an adequate increase of stroke work so that a pathological elevation of venous pressure may not be present The development of clinical venous hypertension may be indicative of abnormal ventricular function

Clinically and experimentally it appears that this type of stress is far less demanding of the ventricle than is the stress of outflow obstruction The work required to pump large quantities of blood through normal orifices is less than that required to overcome resistance to outflow Thus aortic stenosis is more apt to produce clinical evidence of heart failure than is either aortic insufficiency or mitral insufficiency

The hemodynamic alterations associated with other diseases in which cardiac output is increased the hyperkinetic states are discussed in Chapter 5

An intriguing problem is the *effect of prolonged excessive work loads on the heart* As has been pointed out cardiac output may be maintained at normal levels albeit at a slightly higher than normal filling pressure when there is an increased work requirement of either ventricle Such a requirement may stem either from increased resistance to outflow or from increased requirements for total flow With time the ventricle becomes hypertrophied and possibly shifts to a higher ventricular function curve and so it works harder than is normal for the level of filling pressure

Why does the laboring heart ever shift to a failing ventricular function curve? That this need not occur is indicated by patients with pulmonic stenosis and severe right ventricular hypertension who never develop right ventricular failure and by individuals with aortic stenosis or essential hypertension who never develop left ventricular failure It is possible that one solution concerns the quality of the blood supply to the myocardium relative to its metabolic needs The burdened heart contracting against a high resistance requires large amounts of oxygen and hence of coronary blood flow If the blood

supply becomes inadequate the ventricular function may change into that characteristic of the failing heart

Myocardial failure may not be permanent A hypertensive patient who has a cerebral vascular accident and reduction of blood pressure may no longer require digitalis after coronary occlusion ventricular function may be poor only to improve as collateral vessels grow to the myocardium, valvulotomy may reverse the right ventricular failure resulting from pulmonary stenosis There are many other examples suggesting that myocardial failure defined in terms of abnormal ventricular function is dependent upon the balance between cardiac work and myocardial blood supply and is not necessarily irreversible (Fig 15) It is also possible that other factors may be equally or more important in the pathogenesis of myocardial failure and that excessive work loads may per se lead to biochemical or structural changes in the myocardium which are reflected in abnormal ventricular function

Obstruction to Ventricular Inflow

Heart failure as defined at the beginning of this chapter may be caused by obstruction to ventricular filling yet myocardial function may be entirely normal Mitral stenosis the most common example of this abnormality is discussed in some detail in Chapter 5 in which it is pointed out that all of the manifestations of congestive heart failure dyspnea pulmonary congestion edema and elevated venous pressure may result from mitral obstruction in the presence of normal ventricular function

Myocardial Disease

The last group of general causes of heart failure is comprised of conditions in which the primary abnormality is in the heart muscle Myocardial weakness whether due to acute infection rheumatic fever myocardial ischemia or trauma leads to heart failure because for a given stretch the heart does not contract with normal force Severe acute disturbance leads to severe diminution of cardiac output and the heart stops beating or fibrillates either because of the primary involvement or because of reduced coronary flow Less severe chronic diseases are associated with a low cardiac output and

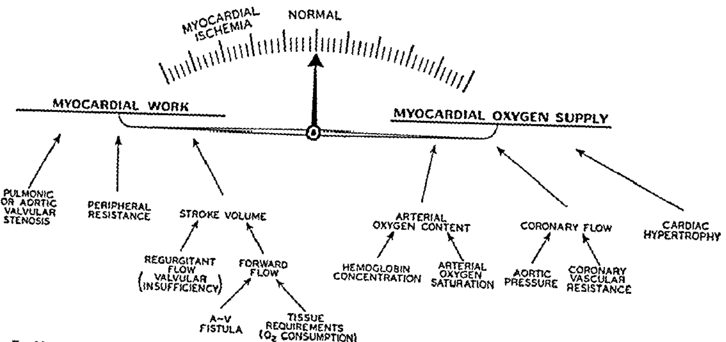


Fig 15 Schematic summary of the factors involved in myocardial ischemia and hence possibly related to myocardial failure Myocardial ischemia occurs when myocardial work the product of cardiac output times resistance to outflow exceeds myocardial oxygen supply in turn a product of coronary blood flow and arterial oxygen content Myocardial hypertrophy may permit more than normal work for a given myocardial oxygen supply

high venous pressure which cause the clinical manifestations of congestive heart failure

TESTS OF MYOCARDIAL FUNCTION

Consideration has been given to the types of stress which may lead to heart failure defined in terms of systemic blood flow It has become evident that abnormal myocardial function may play little or no part in the development of heart failure How may ventricular function be defined in a patient so that the role of the myocardium in the genesis of signs and symptoms of diseases can be assessed? The range of normal for human ventricular function curves is great and largely undefined but if one obtains values for stroke work and atrial pressure it is possible to assess myocardial function A high end diastolic pressure in the ventricle or in the absence of stenosis of the atrioventricular valve a high mean atrial pressure suggests the presence of myocardial failure if stroke work is normal or reduced By the same token subnormal stroke work in the presence of normal atrial pressures is presumptive evidence of myocardial failure

Since only the failing ventricle has a descending limb on its ventricular function curve the finding of decreased stroke work during exercise or after a rapid intravenous infusion represents definitive evidence of a failing myocardium If sequential data are available a lower stroke work than that measured previously at the same or higher filling pressure indicates the development of myocardial failure Finally and of practical value an increase of the cardiac output after the administration of digitalis is a useful sign of a failing ventricle

Heart Rate During Exercise

So far the discussion of cardiac function has centered around stroke volume and stroke work particularly as related to the filling pressure Actually the heart rate is a major determinant of cardiac output the ultimate goal of cardiac function (Chap 1) In normal human subjects the increased blood flow during mild exercise is largely the result of an increased heart rate with little if any increase of stroke volume Normally the heart rate increases linearly with the increased oxygen requirements during muscular exercise The mechanism for this tachycardia has not been defined but it is

likely reflex in origin and serves to maintain adequate tissue oxygen tension (Chap 13) The failing heart with small stroke volume and high filling pressure is apt to exhibit tachycardia perhaps from the same reflexes that operate during muscular exercise in normal hearts The tachycardia may be present at rest and is excessive during muscular exercise During exercise, the heart rate may even be so fast as to curtail diastolic filling and actually cause a fall of cardiac output

SIGNS AND SYMPTOMS OF HEART FAILURE

In the course of the foregoing allusion has been made to some of the signs and symptoms of heart failure of which edema dyspnea and fatigue are particularly important Edema is but one manifestation of systemic venous congestion other signs including venous distention ascites and hepatomegaly This congested state is now known to be associated with an increased extracellular fluid volume due to renal retention of salt and water It may be produced in normal subjects by the administration of large doses of steroids It may occur in patients with nephritis or with mitral stenosis who have normal ventricular function The mechanism of its development in heart disease has led to a great deal of study and controversy Some have felt that increased venous pressure was the primary cause of edema whereas others have felt that the primary factor was a reduced cardiac output As is often the case both sides are right Ample experimental evidence attests to the fact that acute elevation of venous pressure even in veins below the kidney may lead to renal retention of salt and water On the other hand renal retention of salt and water may precede the rise of venous pressure and may be the result of reduced renal blood flow or of the internal secretion of aldosterone or other hormones It is at this point that the definition mentioned at the beginning of this chapter becomes useful—if blood flow is inadequate for the needs of the various organs renal retention of salt and water may ensue This may be a direct effect on the kidney or may be due to hormonal action but a common denominator appears to be inadequate blood flow An interesting notion offered by Epstein is that the stimulus to salt and water retention is inadequate arterial filling This may occur in arteriovenous fistula (Chap 5) when an excessive amount of blood flows through the fistula at the expense of the rest

of the arterial system It has been likened to an internal dehydration reaction leading to compensatory salt and water retention by the kidneys In a similar vein, Peters has suggested that salt and water retention from increased venous pressure is due to dehydration of the rest of the body because of sequestration of fluid out of the vascular system into the tissues in which the venous pressure is high According to this view, elevated venous pressure leads to transudation of fluid into the tissues causing a decrease of total blood volume, which is combated by renal retention of salt and water

Regardless of mechanism inadequate blood flow to the tissues appears to be a stimulus to salt and water retention by the kidney, as does venous congestion so that either abnormality may provoke and perpetuate the formation of edema fluid As mentioned earlier the presence of edema venous congestion or even of cardiac enlargement does not necessarily mean that myocardial failure is present Although the congested state does result from many types of heart disease it may also result from noncardiac factors and may be associated with normal cardiac function Finally it may result from increased venous pressure and/or inadequate cardiac output in the presence of a heart which is burdened but operating on a normal ventricular function curve

A major manifestation of the congested state is elevation of the venous pressure clinically obvious as distended veins A number of studies have indicated that this is not entirely the result of increased blood volume and elevated end diastolic pressure in the ventricle There is evidence that increased venomotor tone plays a part The administration of ganglionic blocking agents may cause reduction of venous pressure presumably by decreasing the venous tone so that the veins accommodate the same volume of blood at a lower pressure (see Chap 1 Venous Pressure) The pathogenesis and importance of increased venomotor tone in producing elevation of venous pressure requires further study

Chapter 12 *is devoted to a discussion of dyspnea The third prominent* symptom of heart failure is fatigue This requires little discussion but it may be a prominent and distressing symptom in patients in whom the cardiac output is inadequate to meet the oxygen requirements of the exercising muscles The pathogenesis of this symptom is not clear but it is probably related to tissue hypoxia It may be the

result of accumulation of metabolic products of anaerobic metabolism Like angina pectoris (Chap 5) it may be useful in setting a limit to the amount of exercise that a cardiac patient can perform with safety

TREATMENT

The treatment of heart failure includes measures aimed at improvement of ventricular function at reduction of the work requirements of the failing ventricle and at relief of associated symptoms The control of the congested state by diuretics and salt restriction may also improve ventricular function Reversal of anemia or hypoxemia may improve ventricular function and also reduce cardiac work requirements

Improvement of Ventricular Function—Digitalis

The drug for the treatment of impaired ventricular function is digitalis This drug has a positive inotropic effect on the myocardium so that the force of contraction is increased In addition digitalis appears to act upon the peripheral vascular bed so that blood is diverted from the central veins into other parts of the vascular bed In normal subjects the net effect of these actions is reduction of the cardiac output In individuals with venous hypertension due to myocardial failure, the peripheral action of digitalis and the inotropic effect act together to cause an increased cardiac output

In the absence of atrial fibrillation in which the ventricular rate is a convenient guide to the adequacy of digitalization the proper administration of digitalis may be difficult Since direct evidence of optimal ventricular function is not available to the physician it is frequently necessary to give the drug to the point of toxicity and then to reduce to maintenance doses just short of this level Recurrence of clinical symptoms may require repetition of this procedure unless the symptoms are sufficiently clear cut and reversible to serve, themselves as an index of the adequacy of digitalization

Digitalis causes a decreased cardiac output if myocardial failure is not present In addition it causes an increase of systemic blood pressure As a result its use should be restricted to patients with myocardial failure or with arrhythmias such as atrial fibrillation It should not be used in every patient with pulmonary or systemic venous congestion, but only when the venous congestion is due to myocardial failure or to a controllable arrhythmia

Reduction of Myocardial Work Requirements

Myocardial work requirements may be reduced (1) by reduction of increased vascular resistance pulmonary or systemic (2) by correction of valvular stenosis or insufficiency or (3) by treatment of abnormalities such as thyrotoxicosis hypoxemia anemia, or arteriovenous fistula which cause increased demands for blood flow (Chap 5) A more general form of therapy is bed rest and sedation Decrease of tissue oxygen requirements effectively reduces the cardiac work load and patients with congestive heart failure respond well to bed rest After compensation has been achieved, such patients should be restricted to a level of activity which can be tolerated without the development of signs or symptoms of heart failure A more extreme form of this type of therapy is the medical or surgical induction of hypothyroidism which may sufficiently reduce myocardial work requirements to restore compensation to the disabled cardiac patient

Relief of Symptoms

Treatment of the signs and symptoms of congestive heart failure may lead to improved myocardial function When dyspnea is relieved by reduction of the work of breathing the oxygen requirements of the respiratory muscles are reduced This cuts down the work required of the heart Abolition of pulmonary edema has a similar effect and improves mycardial function if hypoxemia is abolished Treatment of the congested state with diuretics causes reduction of blood volume and hence of central venous pressures If the heart has been operating on the inefficient descending limb of a ventricular function curve stroke work and cardiac output will increase In order to maintain patients free of venous congestion a sound practice is to have them keep a careful daily weight record and report any sudden gain so that diuretics may be given promptly before edema actually appears The availability of potent oral diuretics has made possible edema free existence for many cardiac patients without the rigorous salt restriction previously necessary

REFERENCES

ALBERT R. E. and EICHNA L. W The response of the peripheral venous pressure to exercise in congestive heart failure *Am Heart J 43* 395 1952

ALBERT R. E SMITH W W and EICHNA L. W Hemodynamic changes associated with fluid retention induced in noncardiac subjects by cortico-

tropin (ACTH) and cortisone comparison with the hemodynamic changes of congestive heart failure *Circulation 12* 1047 1955
BARGER A C Pathogenesis of sodium retention in congestive heart failure *Metabolism 4* 480 1956
BLAIN J M SCHAFER, H SIEGEL A L and BING R J Studies on myo cardial metabolism VI Myocardial metabolism in congestive failure *Am J Med 20* 820 1956
CASE R B BERGLUND F and SARNOFF S J Ventricular function II Quantitative relationship between coronary flow and ventricular function with observations on unilateral failure *Circulation Res 2* 319 1954
COTTON M DE V and STOPP P E Action of digitalis on the nonfailing heart of the dog *Am J Physiol 192* 114 1958
EICHNA L W *et al* Cardiovascular dynamics blood volumes renal functions and electrolyte excretions in the same patients during congestive heart failure and after recovery of cardiac compensation *Circulation 7* 674 1953
EPSTEIN F H POST R S and McDOWELL M The effect of an arteriovenous fistula on renal hemodynamics and electrolyte excretion *J Clin Invest 32* 233 1953
FARBER S J BECKER W H and EICHNA L W Electrolyte and water excretions and renal hemodynamics during induced congestion of the superior and inferior vena cava of man *J Clin Invest 32* 1145 1953
FRIEDBERG C Fluid and electrolyte disturbances in heart failure and their treatment *Circulation 16* 437 1957
GOLDMAN R and BASSETT S H The relationship of sodium retention and venous pressures to edema formation *Circulation 12 630 1955*
HARVEY R M FERRER M I CATHCART R RICHARDS D W JR and COURNAND A Some effects of digoxin upon the heart and circulation in man Digoxin in left ventricular failure *Am J Med 7* 439 1949
HOLLANDER W and JUDSON W E The relationship of cardiovascular and renal hemodynamic function to sodium excretion in patients with severe heart disease but without edema. *J Clin Invest 35* 970 1956
KATZ L N The mechanism of cardiac failure *Circulation 10* 663 1954
OLSON R E Molecular events in cardiac failure *Am J Med 20* 159 1956
ORGAIN E S and STEAD E A JR Congestive heart failure *Circulation 16* 291 1957
RICHARDS D W JR Dynamics of congestive heart failure *Am J Med 6* 772 1949
SAMET P FRITTS H W FISHMAN A P and COURNAND A The blood volume in heart disease *Medicine 36* 211 1957
SMITH H W Salt and water volume receptors An exercise in physiologic apologetics *Am J Med 23* 623 1957
WOOD J E LITTER J and WILKINS R W Peripheral venoconstriction in human congestive heart failure *Circulation 13* 524 1956

CHAPTER 5

ACQUIRED HEART DISEASE

DISEASE OF THE MITRAL VALVE

The normal mitral orifice has an area of 4 sq cm during diastole and is completely occluded by the valve cusps during systole Rheumatic involvement may cause either retraction of the cusps and mitral insufficiency or fusion of the cusps and narrowing of the valve orifice i e mitral stenosis The mitral valve is the commonest site of rheumatic involvement in the heart but there may be coexistent impairment of the aortic or rarely the tricuspid valve Of the two types of disease of the mitral valve mitral stenosis is more serious in terms of morbidity and mortality

PATHOGENESIS

The pathogenesis of mitral stenosis and mitral insufficiency is incompletely understood It is not clear whether valvular abnormality results from continuing rheumatic activity or from slowly progressive scarring after an attack of rheumatic fever The latter is the more likely hypothesis Since the former possibility cannot be excluded every patient who has or has had acute rheumatic fever should receive a course of intensive penicillin therapy to eradicate any streptococcal infection that may be present The development of mitral stenosis or insufficiency becomes increasingly likely with each subsequent attack of rheumatic fever Therefore patients who have had rheumatic fever should probably be placed on prophylactic antibiotic therapy after the initial course of intensive treatment

Auscultatory evidence of abnormality of the mitral valve may be evident soon after the onset of the acute attack of rheumatic fever but symptoms do not usually appear until several years later Thus although rheumatic fever is commonest during the teens the mani

festations of mitral disease, aside from the physical findings, usually do not appear until the fourth decade

MITRAL STENOSIS

Diagnosis

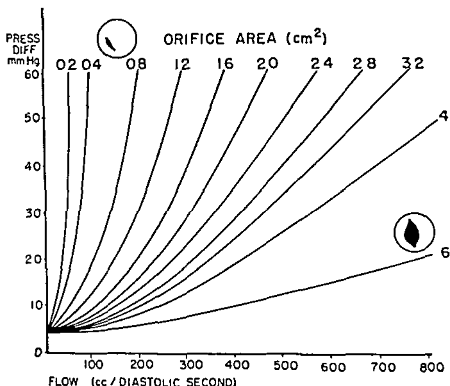
During the past ten years a great deal of information has been obtained about the natural history of mitral stenosis how narrowing of the mitral valve results in disorder of cardiopulmonary function and how this may be modified by commissurotomy In no other cardiopulmonary disease is the intricate interrelationship between the heart and lungs more clearly illustrated Many of the symptoms stem from pulmonary abnormalities resulting from mitral block Secondary reduction of the pulmonary vascular bed may in turn lead to right ventricular failure

Mitral stenosis is usually diagnosed easily by auscultation Characteristic findings are a presystolic crescendo murmur, a loud snapping first sound at the apex (M1) and evidence of pulmonary hypertension, a loud P2 Some patients, particularly those with the greatest degree of stenosis, may not present the typical auscultatory findings With the advent of atrial fibrillation, the crescendo quality of the presystolic murmur is generally lost The murmur may even disappear if the cardiac output becomes so reduced that the rate of blood flow across the mitral valve becomes very slow If calcification develops the opening snap may disappear Under these circumstances, physiological study may be necessary to establish the diagnosis This involves simultaneous measurement of the left atrial and ventricular pressures during diastole (Chap 2) the presence of a pressure gradient being diagnostic of mitral stenosis Such studies are also useful in establishing the degree of stenosis which is not reflected in the intensity of the diastolic murmur

Pathophysiology and Symptoms

PULMONARY CAPILLARY HYPERTENSION The primary effect of mitral stenosis is elevation of the left atrial and, hence, of the pulmonary capillary pressure As illustrated in Figure 16 progressive decrease of valve area is associated for a given cardiac output, with progressive increase of the pulmonary capillary pressure A small degree of narrowing of the mitral valve has little effect on pulmonary capillary pressure, but as the valve gets smaller and smaller, further

narrowing is associated with greater and greater rise of the pulmonary capillary pressure The effect of mitral stenosis on the pulmonary capillary pressure is modified by the level of the cardiac output and of the heart rate Increase of the cardiac output is associated with an increase of the gradient across the mitral valve (Chap 1) and hence elevation of the pulmonary capillary pressure Thus, when



F g 16 Relat onsh p b twe n p u e g adient across the mitral val e and blood flow in v ry ng deg s of m t al stenosis Th p ess re g ad t ses sha ply with a sl ght c eas of blood flow in se e e m tral steno whe eas a large flow must b pr nt befo e an abnormal grad ent d velops in m ld case (F om Rushmer *Card ac Diag osis* Ph ladelphia S und s 1955)

the mitral valve area is reduced to 2 sq cm the pulmonary capillary pressure may be normal at rest but high during exercise Further stenosis is associated with pulmonary capillary hypertension at rest

In some individuals the resting cardiac output falls The mecha nism for this is unknown but the result is reduction of the pulmonary capillary pressure There is evidence indicating that the cardiac out

put is so regulated as to keep the pulmonary capillary pressure below 30 mm Hg the level at which pulmonary edema develops Thus the level of the pulmonary capillary pressure need not reflect the degree of narrowing in severe mitral stenosis, since reduction of the cardiac output may keep the pressure below 30 mm Hg as the stenosis becomes increasingly severe

Tachycardia causes an increase of the pulmonary capillary pressure because blood flows across the mitral valve only during diastole If tachycardia develops, the total time during which blood can flow is greatly diminished and thus, for a given cardiac output, the rate of flow during the shortened diastolic period must be increased This in turn requires elevation of the left atrial pressure to produce the same minute flow

Elevation of the pulmonary capillary pressure leads to transudation of fluid from the pulmonary capillaries If sufficiently severe, this becomes pulmonary edema The engorgement of the pulmonary blood vessels causes reflex tachypnea and increased work of breathing both of which contribute to dyspnea (Chap 12) Patients with dyspnea due to mitral stenosis generally reveal tachypnea and, as a result a low arterial carbon dioxide tension

Not uncommonly pulmonary edema develops after a period of excitement or emotional stress It is probably due to increased capillary pressure secondary to tachycardia and/or increase of the cardiac output Similarly the onset of dyspnea frequently coincides with the advent of rapid atrial fibrillation

Recumbency causes some of the blood in the systemic venous system to be shifted to the pulmonary vascular bed This may cause elevation of the pulmonary capillary pressure to symptomatic levels The result is orthopnea Pulmonary edema has even developed in these patients following a long period recumbency such as occurs during cardiac catheterization

Hemodynamic studies reveal elevation of the pulmonary artery pressure and normal or reduced cardiac output The pulmonary hypertension may be entirely the result of pulmonary capillary hypertension or may be partly due to reduction of the pulmonary vascular bed this in turn may be partly due to pulmonary arteriolar constriction which may be diminished by hexamethonium or other drugs (see below Pulmonary Vasoconstriction) Exercise is associated

with increase of the pulmonary artery pressure and an increase though usually to subnormal levels of the cardiac output

PULMONARY VASCULAR CHANGES The patient with mitral stenosis may learn to live with his disease and to avoid situations which lead to excessive rise of pulmonary capillary pressure This coupled with reduction of the cardiac output may lead to a relatively asymptomatic period However, prolonged pulmonary capillary hypertension often leads to anatomical changes intimal hypertrophy and muscular thickening in the small blood vessels of the lungs with a resultant increase of the pulmonary vascular resistance That these changes are protective to the capillaries is debatable The increased work required of the right ventricle may be a factor in the reduced cardiac output and hence reduced pulmonary capillary pressure but aside from this the increase of pulmonary vascular resistance cannot very well protect the capillaries The pressure in the capillaries is in the last analysis dependent upon the mean pressure in the left atrium The pulmonary arteriolar resistance can affect this only indirectly

The pathological changes that occur in the lungs now become matters of primary concern The resistance to pulmonary blood flow represents a load on the right ventricle which may fail and con tribute to the development of peripheral edema (Chap 4) In addition prolonged pulmonary congestion leads to pulmonary fibrosis which increases the work of breathing Along with loss of the alveolar capillary surface area consequent to obstruction of small blood vessels pulmonary fibrosis leads to reduction of the diffusing capacity of the lungs This may accentuate the hypoxemia already present because of pulmonary congestion At this stage symptomatic deterioration is apt to be accelerated and the opportunity of inducing improvement by commissurotomy is limited Physiological study reveals marked pulmonary hypertension low cardiac output and low diffusing capacity Exercise causes marked increase of the pulmonary artery pressure with little increase of cardiac output and of diffusing capacity The vital capacity is generally reduced hypoxemia is usually present and the arterial P_{co} is usually normal or reduced

PULMONARY VASOCONSTRICTION A number of investigators feel that pulmonary vasoconstriction may be an important factor in the

increased pulmonary vascular resistance found in many patients with mitral stenosis This feeling is based on the facts that (1) the pulmonary vascular resistance often falls immediately after successful commissurotomy and appears to be related to the height of the left atrial pressure, and (2) the administration of drugs such as acetylcholine and hexamethonium may lead to decrease of the pulmonary vascular resistance Some feel that the vasoconstriction is a reflex result of left atrial hypertension, whereas others feel that it is due to local alveolar hypoxia and that it serves to prevent systemic hypoxemia The latter theory is based on the observation that acetylcholine not only lowers pulmonary vascular resistance but also causes a reduction of the arterial oxygen saturation According to the theory hypoxic alveoli are underperfused with venous blood because of local reflex vasoconstriction and so reduced amounts of unoxygenated blood flow from these poorly ventilated areas to mix with well oxygenated blood from the rest of the lungs On administration of acetylcholine which is thought to abolish this vasoconstriction relatively more blood flows through these areas and mixes with the arterialized blood from the rest of the lung to cause hypoxemia

Since the effects of the drugs mentioned above are variable and largely unpredictable, and since in experimental animals and in man hypoxia is at best a mild inciter of pulmonary vasoconstriction it is difficult to be convinced that vasoconstriction is an important factor in the pathogenesis of pulmonary hypertension in mitral stenosis But it may be present and may explain the occasional dramatic fall of pulmonary artery pressure that follows commissurotomy

Commissurotomy

Selection of Patients When should commissurotomy be done? In the early stage, before the development of pulmonary complications, the setting is ideal for the surgeon Irreversible changes have not occurred in the lungs although pulmonary hypertension may be present Given a patient with known reduction of the area of the mitral valve and known absence of severe pathologic changes in the pulmonary arterioles is commissurotomy justified? Unanticipated mitral insufficiency evaluation of which has not yet reached a state of perfection or severe calcific narrowing of the mitral valve may make restorative surgery impossible With improving techniques of

open heart surgery these matters may be better handled in the future There is also a surgical risk The major risks, in addition to those attending any thoracotomy, are embolism from the atrium in advertent rupture of the atrial wall during fracture of the valve and the creation of mitral insufficiency In regard to embolism, particularly apt to occur in patients who are fibrillating the risk may be minimized by the use of anticoagulants before during and after surgery In any event since restorative surgery cannot be guaranteed the risk is such that the decision for mitral commissurotomy is a highly individualized matter depending in large measure on the extent of the patient s symptoms and the experience of the surgical team This is complicated by the fact that the patient with early symp toms may be maintained by medical management for many years al though there is a strong likelihood that these symptoms would even tually progress to the point where surgery can no longer offer as much

In patients with pulmonary vascular disease the amount of benefit that may accrue from successful commissurotomy is often not as great as might be desired Pulmonary hypertension is often reduced par ticularly if very severe preoperatively but generally not abolished Clinical improvement is often much greater than the measurable hemodynamic effects of surgery Evidence is accumulating to the effect that the pulmonary artery pressure reduced immediately after surgery may rise again in two to five years in some patients At present it seems that patients who are disabled by mitral block represent legitimate candidates for surgery despite the presence of pulmonary vascular disease Patients with milder symptoms must be evaluated carefully and individually Patients with advanced pul monary fibrosis represent poor operative risks and can have little hope for improvement from commissurotomy

Physiological Studies Many patients with clear cut signs of mitral stenosis and resulting symptoms of disability require no physiological study and may be adequately evaluated for surgery on clinical grounds alone In other cases physiological study is very useful In some cases if the mitral diastolic murmur is absent or atypical left heart catheterization may be necessary in order to establish the diagnosis In other cases with typical signs of mitral stenosis it may be difficult to decide whether or not the mitral block

is actually causing difficulty In such cases, demonstration of pulmonary hypertension by right heart catheterization provides a clear cut indication for surgery, whereas if the pulmonary artery pressure remains normal during exercise there is probably no need for surgery Studies of exercise tolerance are somewhat simpler to perform and may provide useful information Reduction of exercise tolerance or excessive tachycardia during exercise suggests that a functional limitation is present and that surgery may be indicated Such studies are particularly useful if performed serially on a patient The appearance of abnormality in a previously normal subject is convincing evidence that surgery should be performed Studies of pulmonary function are useful in that the demonstration of reduced lung volumes and of marked impairment of diffusion of gases in the lungs suggests the presence of pulmonary fibrosis which entails increased risks of surgery and a reduced likelihood of achieving benefit from successful commissurotomy Finally physiological study may be necessary in order to evaluate the role of mitral insufficiency and of left ventricular failure in the genesis of an individual patient s symptoms

MITRAL INSUFFICIENCY A particularly important problem in the evaluation of the patient for commissurotomy is the distinction between mitral stenosis and mitral insufficiency With improving techniques for open heart surgery this distinction may become academic since the surgeon may eventually be prepared to correct either type of lesion At the present time however it is important to exclude dominant mitral insufficiency before subjecting a patient to commissurotomy Patients with combined lesions present the most difficult problems Pure mitral stenosis with a valve less than 1 sq cm in area, is generally not associated with a systolic apical murmur Left heart catheterization reveals a pressure gradient across the mitral valve during diastole and a typical pressure pulse in the left atrium with a very slow descent of the 'y wave If pure mitral insufficiency is present with a valve area greater than 2 sq cm , the diastolic apical murmur is often absent and there is no pressure gradient across the mitral valve during diastole In combined lesions, with intermediate sizes of the mitral valve the decision as to which is the hemodynamically significant lesion and whether or not it can be corrected is difficult One may partially quantitate as described in

Chapter 2 the severity of each lesion but one may not predict to what extent surgery is possible In such patients, operation is generally advised if symptoms are severe, with the knowledge that surgery may be exploratory and that definitive improvement may not be possible Such patients might well be treated medically until the advent of satisfactory open heart surgery makes possible reconstructive surgery of any lesion found

LEFT VENTRICULAR FAILURE Recently Ferrer and associates have indicated that it is important to exclude myocardial failure as the cause of a patient s signs and symptoms before attempting valvular repair In patients with a small heart on x ray this distinction is usually not difficult mitral stenosis being the important lesion However some patients with mitral stenosis suffer primarily from left ventricular failure As in mitral insufficiency left ventricular failure with pulmonary capillary congestion may lead to the same pulmonary vascular changes as those seen in mitral stenosis so that pulmonary hypertension may be present However left ventricular failure is usually characterized by an enlarged left ventricle and on physiological study by a low cardiac output and relatively less pulmonary hypertension than that seen in mitral stenosis Exercise is more apt to result in an increase of the cardiac output in mitral block than in left ventricular failure and the pulmonary hypertension during exercise is generally but not always more severe in mitral block than in left ventricular failure These parameters provide suggestive leads but are not diagnostic Measurement of an elevated left ventricular end *diastolic pressure is definitive evidence of left ventricular failure* Finally the response to the administration of digitalis may be helpful As mentioned in Chapter 4 the failing myocardium responds to the administration of digitalis with an increase of cardiac output and a decrease of end diastolic ventricular and mean atrial pressure In mitral block the cardiac output does not change or it falls and pressures do not change after digitalization Rapidly acting acetyl strophanthidin is a useful agent for testing patients in this way Increase of the cardiac output after administration of this drug is evidence of left ventricular failure

The demonstration of left ventricular failure need not absolutely preclude attempted surgical correction of known coexistent mitral

stenosis Insufficient experience has been obtained on this point, but it has not been proved that myocardial function will not improve after successful commissurotomy On the other hand demonstration of hemodynamic left ventricular failure would appear to represent a relative contraindication to surgery

Medical Treatment

The management of the patient in the early stage of mitral stenosis is largely supportive Exercise sufficient to produce symptomatic elevation of the pulmonary capillary pressure should be avoided Treatment of pulmonary edema, the end result of severe pulmonary capillary hypertension, is discussed in Chapter 10 and includes (1) measures aimed at shifting the blood from the lungs into the systemic vascular bed tourniquets and possibly ganglionic blocking agents and (2) measures aimed at treating the pulmonary edema per se morphine and oxygen under inspiratory positive pressure

The advent of atrial fibrillation alters the picture of mitral stenosis in two particular ways In the first place a fibrillating atrium is very apt to be the site of thrombus formation which may cause systemic embolization A recent trend of suggestive but unproved value is to treat all patients with atrial fibrillation with anticoagulants on a long term basis In addition the rapid heart rate due to atrial fibrillation results in left atrial hypertension (see above) so that the first bout of pulmonary congestion may appear with the onset of fibrillation Although the fibrillation may be changed to normal sinus rhythm with quinidine, permanent restoration of regular sinus rhythm is often difficult and a common approach is to control the ventricular rate with digitalis and not to be concerned about the presence of fibrillation

There are two main indications for treating a patient having mitral stenosis with digitalis Rapid atrial fibrillation is one Right ventricular failure secondary to pulmonary hypertension is the other Pulmonary congestive symptoms in the absence of fibrillation should probably not be treated with digitalis, since they result from obstruction to the flow of blood through the mitral valve and the degree of mitral block is unaffected by digitalization Hemodynamic studies have consistently revealed that digitalis is without salutary effect in patients with mitral block and normal sinus rhythm

MITRAL INSUFFICIENCY

Pathophysiology

Often a benign lesion, mitral insufficiency is characterized by a loud systolic apical murmur This is, however a common physical finding and often not indicative of organic mitral insufficiency Systolic regurgitation of blood through the mitral valve imposes a hemodynamic burden on the left ventricle which may eventually fail (Chap 4) Frequently however adequate compensation is present and so a large degree of insufficiency may be tolerated without clinical symptoms

This lesion may cause an increase of the pressure in the left atrium particularly during systole with resultant pulmonary vascular changes similar to those occurring in mitral stenosis These in turn may lead to pulmonary hypertension and right ventricular failure identical to that occurring in mitral stenosis Under these circumstances the left ventricular enlargement associated with left ventricular failure may be hard to distinguish from right ventricular enlargement Left heart catheterization may be necessary to distinguish such a patient from one with mitral stenosis

An uncommon result of mitral insufficiency is the development of massive enlargement of the left atrium This often occurs without other hemodynamic complications and does not necessarily alter the relatively benign prognosis of mitral insufficiency The reason for its development it not clear perhaps it is related to the jet action of the regurgitant blood hitting the atrial wall It may actually press on the spine and produce back pain Amputation though technically feasible is rarely required

Treatment

The medical management of mitral insufficiency centers about the treatment of left ventricular failure (Chap 4) It may be necessary to curtail activity in order to keep the forward flow requirements within the limits of the laboring myocardium Digitalis should be used for left ventricular failure Anticoagulants may be indicated for the treatment of patients with atrial fibrillation just as in mitral stenosis At the present time surgery for mitral insfficiency is largely in the exploratory stage Definitive operative correction may be possible in the near future

DISEASE OF THE AORTIC VALVE

Although the degree of aortic stenosis and insufficiency may be quantitatively assessed by left heart catheterization (Chap 2) surgical treatment is at present of such dubious value that a recommendation for surgery is generally based on the presence of severe symptoms Physiological study often plays little part in the evaluation or treatment of a given patient, though left heart catheterization is probably essential before aortic valvulotomy in order to make sure that aortic stenosis is present

AORTIC INSUFFICIENCY

Rheumatic fever or syphilis may lead to retraction of the cusps of the aortic valve and to the development of valvular insufficiency This means that blood regurgitates back from the aorta into the left ventricle during diastole after the aortic valve has closed This causes a characteristic high pitched diastolic murmur to the left of the sternum As is the case with other valvular lesions, the intensity of the murmur bears no relationship to the degree of insufficiency

The consequences of aortic insufficiency relate to the fact that part of each left ventricular stroke volume flows backwards into the ventricle during diastole The degree of regurgitation is dependent upon the degree of cusp retraction Since blood enters the ventricle both from the aorta as well as from the atrium during diastole end diastolic volume is greater than normal and as predicted by the Starling relationship (Chap 1) stroke work is increased Since the mean arterial pressure is normal this means that stroke volume is increased As a result an adequate forward flow is maintained

There is another compensation that maintains an adequate forward flow in aortic insufficiency Physiological studies have shown that the time of isometric contraction is shortened whereas the period of systolic emptying is increased Thus more of each systole is utilized for the ejection of blood

In patients with aortic insufficiency the heart becomes hypertrophied and presumably more powerful This chronic adjustment to the increased flow load may permit increased stroke work at a normal filling pressure Along with the adjustments mentioned above this permits normal forward flow during muscular exercise despite the fact that a large fraction of each systolic ejection flows backward into the ventricle

The increased flow requirements in aortic insufficiency are met with surprising ease presumably by means of the adjustments mentioned above Patients with a large amount of regurgitation may lead normal lives for years Eventually left ventricular failure may develop with elevation of left ventricular end diastolic pressure pulmonary congestion and salt and water retention (Chap 4) When this complex of symptoms occurs it is often the result of coincident aortic stenosis and/or coronary artery disease The latter is particularly deleterious, since the hypertrophied heart of aortic insufficiency requires increased amounts of coronary flow

Medical treatment of aortic insufficiency centers about the treatment of left ventricular failure when it develops That the advent of heart failure may be postponed by avoidance of heavy activity is a matter of debate Certainly some patients lead active lives for many years despite having this lesion but it is possible that indulgence in heavy activity may predispose to the eventual development of myocardial failure (Chaps 4 13) A sensible approach is to restrict these patients to a level of activity that they can tolerate with comfort

Surgical treatment of aortic insufficiency has until recently involved insertion of a plastic Hufnagel valve into the descending aorta thus removing regurgitant flow from the vascular bed below the artificial valve The procedure is at best palliative and is generally reserved for those patients who exhibit evidence of a downhill course generally a rapid one One possible indication for such surgery is the onset of angina pectoris often an ominous prognostic sign Satisfactory improvement may follow surgery but more definitive valvular prostheses remain a real hope for the future

AORTIC STENOSIS

The acquired form of this lesion may follow rheumatic valvulitis or may be due to arteriosclerotic involvement of the aortic valve It increases the work required of the left ventricle for ejection of a normal volume of blood with each heart beat Blood flow through the narrowed valve produces a characteristic murmur and thrill and the aortic second sound is delayed or absent Characteristically the arterial pressure shows a delayed rise with a low anacrotic notch and the pulse pressure is narrowed But arterial pressure tracings are not diagnostic

The adjustments to aortic stenosis have been outlined in Chapter 4

(Obstruction to Ventricular Outflow) and are somewhat similar to those in aortic insufficiency Increased end diastolic volume causes increased stroke work so as to maintain stroke volume through the narrowed aortic valve In addition, the period of isometric contraction is shortened and thus the longer period of systolic ejection provides more time for ventricular emptying The end diastolic pressure in the left ventricle is elevated The myocardium may hypertrophy and thus generate a more forceful systolic contraction with each heart beat

Clinically and as shown by physiological study, aortic stenosis represents a greater load on the myocardium than does aortic insufficiency Generation of large pressures is more of a stress than is production of large flows Patients with aortic stenosis are more apt to develop left ventricular failure and at an earlier age than are those with aortic insufficiency In addition syncope is apt to occur This may be related to the coronary insufficiency which is particularly apt to occur in patients having this lesion because of the increased requirements for coronary flow to the hypertrophied left ventricle and because of the fact that the mean aortic pressure, the coronary perfusion pressure is reduced Any relaxation of the systemic vascular resistance will produce hypotension and aggravate the coronary insufficiency Syncope is a serious prognostic sign and often the precursor of sudden death

Medical management is similar to that outlined above for aortic insufficiency Unfortunately surgery is not much more effective than is surgery for aortic insufficiency Theoretically, surgical splitting of the valve commissures should be just as effective as surgery for mitral stenosis and pulmonic stenosis In practice however, it is extremely difficult to obtain a satisfactory aortic commissurotomy If an adequate split is obtained aortic insufficiency is very apt to result Abolition of the systolic pressure gradient is unusual and generally only a small improvement can be achieved This may be of value, however and a patient with severe stenosis may achieve considerable benefit from a very slight increase of the valve area

Since surgery is far from restorative it is reserved for patients with symptoms such as syncope coronary insufficiency or left ventricular failure Other patients should be managed conservatively until operative procedures are developed for definitive restoration of the aortic valve toward normal Since only symptomatic cases are generally considered for surgery there is little indication for physiological study in the absence of symptoms On the other hand patients with left

ventricular failure and the physical signs of aortic stenosis should be studied They may in fact be suffering from ischemic or other types of heart disease and so physiological study should always be performed preoperatively to make sure that the stenosis is hemodynamically significant and presumably, the cause of the symptoms

A special problem is posed by coexistent aortic and mitral stenosis If mitral commissurotomy is performed the increased diastolic flow into the left ventricle may be overwhelming and cause left ventricular failure As a result the surgeon must be prepared to attack the aortic stenosis The preferred procedure is to perform aortic commissurotomy prior to mitral commissurotomy Patients with combined lesions require much more critical selection for surgery than do patients with either lesion alone

DISEASE OF THE TRICUSPID VALVE

TRICUSPID STENOSIS

Though not common tricuspid stenosis is not as rare as was once believed The result of rheumatic fever it is usually accompanied by disease of the mitral valve The important physical sign is a diastolic murmur just to the left of the sternum which is loudest during inspiration This respiratory variation of the diastolic murmur is not present in mitral stenosis and is due to the fact that the rate of flow of blood into the chest is increased when the intrathoracic pressure is reduced by inspiration This is associated with increased flow of blood across the tricuspid valve but not across the mitral valve Conversely tricuspid but not mitral flow is decreased during expiration Diagnosis is made by measuring a diastolic pressure gradient between the right atrium and right ventricle The major physiological consequence of tricuspid stenosis is elevation of the right atrial pressure and thus of the venous pressure with resultant systemic congestion (Chap 4)

Lukas and associates have presented evidence indicating that the presence of tricuspid stenosis protects the pulmonary capillaries in patients with coexistent mitral stenosis The pulmonary capillary pressure appears to be lower in patients with combined lesions than in those with a comparable degree of mitral stenosis alone This protection probably results from reduction of the cardiac output just as pulmonary vascular changes may protect the lung capillaries by increasing right ventricular work with a resultant decrease of cardiac output On the other hand the increased right atrial pressure accent-

uates the tendency to edema formation, and hence this lesion is of questionable benefit to the patient with mitral stenosis

TRICUSPID INSUFFICIENCY

Tricuspid insufficiency is usually the functional consequence of dilatation of the right ventricle secondary to pulmonary hypertension or pulmonic stenosis The major effect of the lesion is a further in crease of the right atrial pressure, but the underlying cause of the right ventricular dilatation is far more serious than the tricuspid insufficiency per se

ISCHEMIC HEART DISEASE

TYPES

Ischemic heart disease develops when the oxygen supply to the myocardial fibers is inadequate This condition occurs when the cor onary blood flow is insufficient to meet myocardial needs Acute but reversible inadequacy of coronary flow generally induced by in creased myocardial activity like that which occurs in muscular exercise results in chest pain i e angina pectoris Acute severe and irreversible inadequacy of coronary flow generally the result of occlusion of one of the coronary arteries causes myocardial infarc tion Chronic inadequacy of coronary blood flow may result in myo cardial failure Although all three conditions develop only after or ganic reduction of the coronary arterial bed generally by arterioscle rosis the degree of myocardial ischemia is modified by myocardial oxygen requirements arterial blood pressure and the arterial oxygen content (Chap 4 Fig 15)

In this section the factors responsible for maintenance of a normal oxygen tension in the myocardium will be outlined methods available for increasing the coronary blood flow will be discussed and then myocardial infarction and failure will be discussed from the stand point of therapy Although tests of cardiopulmonary function are often of little value in the actual assessment of patients with ischemic heart disease with the exception of those in myocardial failure cardiopulmonary physiology has bearing on the pathogenesis and treatment

CORONARY CIRCULATION

The amount of oxygen available to the myocardial fibers depends upon the amount of oxygen in the arterial blood and upon the blood

flow to the myocardium Hypoxemia (Chap 11) may accentuate myocardial hypoxia but is rarely, if ever responsible for ischemic heart disease If present as a contributing factor, it should be corrected

Ischemic heart disease is generally the result of reduction of the coronary blood flow The latter is dependent upon the mean pressure available for perfusion of the coronary bed the mean aortic pressure and upon the size of the coronary arteries and arterioles offering resistance to blood flow (Chap 1 Mean Pressure Flow and the Volume of Blood in the Circulatory System) Although the level of mean aortic pressure is important in maintaining coronary flow ischemic heart disease is almost always the result of reduction of the size of the perfused vascular bed Systemic hypotension may aggravate myocardial ischemia but unless severe probably does not by itself cause significant myocardial ischemia

Normally the coronary arterioles are capable of dilatation and constriction and their caliber appears to be largely under the control of the myocardial oxygen tension When as in muscular exercise, the heart beats with increased force and consequent increased uptake of oxygen tissue hypoxia causes vasodilatation This increases the coronary blood flow and restores the myocardial oxygen tension toward normal The coronary vascular bed may be decreased by arteriosclerosis so that at rest it is at the point of maximum dilation Under these circumstances vasodilatation does not occur during exercise and myocardial hypoxia results If severe it is associated with angina pectoris

Occlusion of a branch of a coronary artery is followed by hypoxia of the muscle distal to the point of occlusion The degree of infarction beyond the site of the occlusion depends on the extent of pre existent collateral blood vessels available to supply blood to the area distal to the occlusion The presence of a large collateral network such that all myocardial fibers may receive blood from more than one artery affords important protection against the development of myocardial infarction

TREATMENT

Measures Designed to Increase Coronary Circulation

The most potent stimulus to the development of collateral circulation to the myocardium or elsewhere is reduction of the blood supply to the tissues The neural or humoral factors responsible for the

growth of collateral vessels are unknown and the study of this process is a fertile field for research

Many attempts have been made to increase the coronary collateral circulation by surgery In general, most techniques seem capable of inducing approximately 10 per cent increase of flow to the superficial layers of the myocardium Whether or not this is of functional consequence cannot as yet be stated Such a collateral circulation may be produced by rather minor surgical techniques On the other hand convincing data are not at hand to say that the natural history of coronary artery disease is in any way affected by such surgery

A good deal of attention has been given to the possibility that muscular exercise is of benefit to patients with ischemic heart disease Eckstein has shown that the collateral circulation developed faster, after coronary occlusion in exercised dogs than in sedentary dogs This might have application to human subjects except that the level of exercise was by human standards, excessive and the degree of effect was not great The beneficial effect of exercise on promoting collateral circulation which is either of protective or of restorative value to the human ischemic heart remains to be proved

A number of vasodilator drugs are available for the treatment of ischemic heart disease Many agents achieve coronary vasodilatation by increasing the work of the heart and hence by lowering myocardial oxygen tension This is obviously an undesirable *modus operandi* but the net value of such drugs is indicated by their clinical effectiveness in relieving angina pectoris That they have a place in the management of myocardial failure due to ischemic heart disease cannot be said They appear to be of no value in patients with coronary occlusion presumably because the collateral vessels supplying the infarcted myocardium are already at a maximum size as a result of the very low myocardial oxygen tension in the area which they supply

Myocardial Infarction

The management of myocardial infarction is based on the principle that the functional consequences of coronary occlusion must be detected and combated while the patient pursues a regimen of minimal activity to permit healing and restoration of circulation to the damaged myocardium Unfortunately little can be done to hasten this process Until the infarcted myocardium heals with firm scar

tissue, which takes about two weeks, the patient is kept quiet to prevent excessive rise of intraventricular pressure Cardiac rupture has occurred among inmates of mental institutions when the infarction was not diagnosed and the patients pursued their active daily routine

If myocardial infarction is so severe as to produce heart failure with pulmonary or systemic manifestations, treatment with digitalis is indicated The treatment of shock accompanying acute myocardial infarction has received a good deal of attention particularly with respect to the use of transfusion and pressor agents Neither of the latter attacks the cause of the problem—the acutely failing heart Both may raise the blood pressure particularly pressor agents but that this is desirable cannot be stated with certainty Elevation of the blood pressure leads to increased blood flow to the heart as well as to the kidneys and other organs but it is not clear that the augmented coronary flow is more than sufficient to meet the requirements of the increased cardiac work Clinically survival seems to be slightly more assured with this type of treatment

A few words about the use of oxygen in patients with myocardial infarction—what does it accomplish? It is probably indicated because most people expect that it should be used and an oxygen tent emphasizes the severity of the illness to the friends and relatives On the other hand inspiration of 60 per cent oxygen the maximum one can expect in a tent only serves to dissolve about 1 cc of oxygen in every 100 cc of plasma corresponding to about 5 per cent of the oxygen already present in combination with hemoglobin This is certainly not an impressive amount of oxygen However the partial pressure of oxygen in the blood is raised considerably from 100 to more than 300 mm Hg This means that the tendency of oxygen to diffuse out of arterial blood at the arterial end of the tissue capillary is greatly augmented At least a few molecules of oxygen will be driven by this high pressure head into the tissues and this might be of importance to the infarcted myocardium Anginal pain may be relieved by oxygen and there appears to be good reason to use oxygen in acute coronary insufficiency It is probably indicated in myocardial infarction as well

Chronic Ischemic Heart Disease

Treatment of chronic ischemic heart disease involves (1) reduction of the work of the left ventricle to a level which can be met satis

factorily by the coronary circulation (2) treatment of congestive heart failure by diuretics and digitalis (Chap 4), and (3) improvement of the coronary circulation Vasodilator and surgical therapy of the latter have been mentioned Another approach surgical or medical is to induce hypothyroidism in order to diminish the work requirements of the myocardium Although palliation of intractable angina or congestive heart failure may be achieved by this means such therapy is rarely necessary

It is frequently difficult to decide how much activity a patient with ischemic heart disease can tolerate When present angina pectoris serves as a guide and levels of activity which produce chest pain should be avoided Patients without this symptom should also avoid levels of activity at which salt and water retention develop and which are associated with dyspnea and/or fatigue Further research is necessary in order to determine whether or not levels of activity not associated with symptoms are in any way harmful and if so how the harmful level of work may be determined

HYPERTENSIVE HEART DISEASE

Hypertension is due to increased systemic vascular resistance It is a form of obstruction to ventricular outflow (Chap 2) and it causes increased work of the left ventricle The latter is achieved both by increase of the end diastolic pressure in the left ventricle and by left ventricular hypertrophy Hemodynamic studies have indicated that patients who do not have signs or symptoms of heart failure generally have normal myocardial function in terms of work performed at a given filling pressure This is true despite the presence in some cases of a left ventricular strain pattern on the electrocardiogram

Eventually as in aortic stenosis coexistent coronary artery disease may lead to diminution of coronary blood flow which must be excessive in order to maintain the high myocardial requirements for oxygen Myocardial failure may then develop This is certainly not inevitable but is more apt to occur in an individual having hypertension than in a normotensive person since the former demands so much more of his coronary circulation in order to maintain a normal myocardium Until the signs or symptoms of decompensation appear

treatment with digitalis is not indicated and probably should not be used since digitalis increases the systemic vascular resistance and arterial blood pressure

CONSTRICTIVE PERICARDITIS

The diagnosis of constrictive pericarditis may be made from the characteristic clinical picture of persistent venous congestion in the presence of a small heart diminished pulse pressure and diminished cardiac excursion on fluoroscopy Hemodynamic studies have revealed information of basic interest and practical value in the surgical management of the disease Such data may occasionally be of diagnostic value Such studies have shown that pericardial constriction interferes with cardiac function predominantly by limiting the diastolic expansion of the ventricles rather than by obstructing venous return The ventricles are rendered relatively indistensible As a result normal inflow of blood causes an abnormal rise of diastolic pressure Since end diastolic fiber size is subnormal cardiac contractions are not as forceful as normal and systolic pressure is reduced This accounts for the small pulse pressure and diminished cardiac output which are usually present

Since cardiac function is limited by the encasement of the myocardium in a fibrous sheath proper surgical correction requires extensive freeing of the myocardium and not mere removal of the pericardial bands around the atria and great veins Properly performed surgery is followed by increased diastolic filling of the ventricles increased cardiac output and gratifying clinical improvement Without satisfactory surgery the prognosis is grave

Hemodynamic studies may be of value in the differential diagnosis of constrictive pericarditis They may be particularly helpful in excluding myocardial failure and myocardial fibrosis Myocardial failure may be excluded by the finding of no change or a fall of cardiac output after the administration of digitalis Myocardial fibrosis hemodynamically a very similar lesion may be very difficult to distinguish from constrictive pericarditis but constrictive pericarditis is generally associated with a higher mean atrial and end diastolic ventricular pressure and a more characteristic M or W pattern of the pressure in the atrium

HYPERKINETIC STATES

Diseases which have in common an abnormally high cardiac output are classified as hyperkinetic states Of these, thyrotoxicosis anemia arteriovenous fistula (special examples of which are Paget's disease and beriberi) and vasoregulatory asthenia will be discussed here Right heart failure secondary to emphysema is discussed in Chapter 6

THYROTOXICOSIS

In thyrotoxicosis, the increased tissue requirements for oxygen are met by an increase in the cardiac output This is true both at rest and during muscular exercise Although the systemic peripheral resistance is reduced mean systolic pressure is generally elevated This multiplied by the increased cardiac output represents increased work for the left ventricle

Systemic venous congestion may develop in thyrotoxicosis but it is usually due to coexistent heart disease In uncomplicated thyrotoxicosis the increased cardiac output is not accompanied by undue increase of the pressure in the atria even during muscular exercise When the atrial pressure rises additional disease such as ischemic heart disease is usually present

Congestive heart failure and rapid atrial fibrillation due to hyperthyroidism are best treated with antithyroid therapy Digitalis may be of little value until the euthyroid state has been achieved at which point it is no longer necessary unless other disease is present

An interesting contrast is presented by hypothyroidism the pathophysiological opposite of hyperthyroidism In this condition the reduced oxygen consumption is associated with a reduced cardiac output Since the right ventricular end diastolic and right atrial pressures are normal the enlarged cardiac silhouette which may be evident on x ray is usually the result of ischemic heart disease

ANEMIA

In anemia the capacity of the blood for carrying oxygen is reduced in direct proportion to the degree of reduction of the hemoglobin concentration As a result the arterial oxygen content is reduced Tissue oxygen requirements are met by increased cardiac output largely the result of increased stroke volume Since the peripheral vascular resistance is reduced the work of both ventricles may be

normal both at rest and during exercise Atrial pressures are normal at rest and during exercise and myocardial function is normal

However congestive heart failure may develop in anemia Sarnoff has shown that, at moderate work loads ventricular function is ab normal in anemic dogs This is thought to be the result of inadequate myocardial oxygenation and it is reversed by blood transfusion Con gestive heart failure is particularly apt to develop in anemic patients who also have ischemic heart disease Under these circumstances the combined effects of a reduced coronary vascular bed and of reduced arterial oxygen content may lead to abnormal ventricular function Correction of the anemia is an important step toward restoring ven tricular function to normal

An interesting finding in anemia is reduction of the arterial oxy gen saturation Since this may be present even during oxygen breath ing it is probably due to some form of right to left shunt Some investigators have postulated that the shunt is the result of multiple small arteriovenous communications in the lung The presence and extent of these lesions remain to be proved

ARTERIOVENOUS FISTULA

Systemic arteriovenous fistula may be a single lesion in which case it is usually the result of a traumatic wound or many lesions may be present The latter occur in the bone in Paget s disease and in the skin in beriberi The physiological consequence of all types of fistula is the same a large amount of blood flows through the low resistance fistula so that maintenance of adequate flow to the tissues requires increased cardiac output Physiological study has shown that the cardiac output in such patients is indeed elevated both during rest and exercise

The congested state complicating arteriovenous fistula is of great interest The cardiac output is increased and yet the kidneys retain salt and water Epstein has suggested that this is a form of dehydra tion reaction that the filling of the systemic arterial bed is inadequate because so much blood flows through the fistula This decreased in travascular volume leads to renal retention of salt and water The result is edema and venous congestion Data obtained by Gregg and his associates indicate that the congested state in dogs with arterio venous fistula is not due to cardiac failure These animals have a cardiac output which approaches the maximum seen in normal dogs

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the hemodynamic abnormalities in anxiety and in vasoregulatory asthenia seem to be similar

REFERENCES

DISEASE OF THE MITRAL VALVE

ARAUJO J and LUKAS D S Interrelationships among pulmonary capillary pressure blood flow and valve size in mitral stenosis The limited regulatory effects of the pulmonary vascular resistance *J Clin Invest 31* 1082 1952

BALCHUM O J GENSINI G and BLOUNT S G JR The effect of hexa methonium upon the pulmonary vascular resistance in mitral stenosis *J Lab & Clin Med 50* 186 1957

BENTIVOGLIO L URICCHIO J F and LIKOFF W The paradox of right ven tricular enlargement in mitral insufficiency *Am J Med 24* 193 1958

COTES J E The role of oxygen carbon dioxide and lactic acid in the ventila tory response to exercise in patients with mitral stenosis *Clin Sc 14* 317 1955

CURTI P C *et al* Respiratory and circulatory studies of patients with mitral stenosis *Circulation 8* 893 1953

DAVIES L G GOODWIN J F and VAN LEUVEN B D The nature of pulmo nary hypertension in mitral stenosis *Brit Heart J 16* 440 1954

DONALD K W BISHOP J M WADE O L and WORMALD P N Cardio respiratory function two years after mitral valvotomy *Clin Sc 16* 325 1957

ELLIS F H JR KIRKLIN J W PARKER R L BURCHELL H B and WOOD E H Mitral commissurotomy An over all appraisal of clinical and hemodynamic results *A M A Arch Int Med 94* 774 1954

FERRER M I *et al* Circulatory effects of mitral commissurotomy with par ticular reference to selection of patients for surgery *Circulation 12* 7 1955

GOODALE F SANCHEZ G FRIEDLICH A L SCANNELL J G and MYERS G S Correlation of pulmonary arteriolar resistance with pulmonary vascu lar changes in patients with mitral stenosis before and after valvulotomy *Brit Heart J 18* 430 1956

HARVEY R M *et al* Mechanical and myocardial factors in rheumatic heart disease with mitral stenosis *Circulation 11* 531 1955

JUDSON W E HATCHER J D HOLLANDER W and HALPERIN M H The effects of mitral valvuloplasty on cardiovascular and renal function at rest and during exercise *J Clin Invest 34* 1297 1955

LEWIS B M GORLIN R HOUSSAY H E J HAYNES F W and DEXTER L Clinical and physiological correlations in patients with mitral stenosis *Brit Heart J 15* 108 1953

LUKAS D S MAHRER P R and STEINBERG I Angiocardiographic and physiologic correlations in mitral stenosis *Circulation 17* 567 1958

MARSHALL H W WOODWARD E and WOOD E H Hemodynamic methods

acutely loaded with an intravenous infusion Furthermore the cardiac output is not increased by the administration of digitalis

The congested state in patients with arteriovenous fistula may not be affected by the administration of digitalis Relief requires surgical excision of the fistula This is not without hazard The immediate effect of surgery is an increase of the blood pressure, due to the sudden removal of the decreased systemic vascular resistance The increase in blood pressure is followed by reflex bradycardia In patients having a dilated heart, the sudden increase of work load may be overwhelming and symptoms of congestive failure may ensue Subsequently a diuresis will result in a return to normal if the patient can be tided over the immediate postoperative interval Phlebotomy might be helpful at this time

VASOREGULATORY ASTHENIA

Holmgren and associates have recently described a group of patients with cardiac symptoms without clinical or physiological evidence of heart disease Characteristically these patients displayed reduced exercise tolerance and abnormal tachycardia during exertion Physiological studies at rest and exercise revealed normal intracardiac pressures but increased cardiac output The latter was due to the tachycardia and stroke volume was normal With physical conditioning the abnormal hemodynamics returned toward normal

This syndrome is thought to be the result of faulty regulation of peripheral blood flow Apparently there is inadequate vasoconstriction in areas other than the muscles particularly during exercise so that adequate blood flow to the exercising limbs requires an abnormally high cardiac output This is brought about by tachycardia Because of the abnormal peripheral vasoregulation much of the cardiac output is 'wasted' by flowing to areas other than the muscles and so exercise tolerance is reduced This abnormality appears to be reversible by physical training

It is likely that many patients with neurocirculatory asthenia actually suffer from this abnormality Such a diagnosis is suspected in individuals with cardiac symptoms who show no clinical evidence of heart disease but who have tachycardia during exercise The diagnosis may be confirmed by finding a high cardiac output in the absence of anemia, thyrotoxicosis, arteriovenous fistula or pulmonary disease It may be difficult to distinguish this syndrome from anxiety because

GREEN H D Pharmacology of antihypertensive drugs *Am J Med 17* 70 1954

SMITH J R and HOOBLER S W Acute and chronic cardiovascular effects of pentolinium in hypertensive patients *Circulation 14* 1061, 1956

TAYLOR S H DONALD K W and BISHOP J M Circulatory studies in hypertensive patients at rest and during exercise *Clin Sc 16* 351 1957

WIGGERS C J Dynamics of hypertension *Am Heart J 16* 516 1938

CONSTRICTIVE PERICARDITIS

BURWELL C S Constrictive pericarditis *Circulation 15* 161 1957

NYE R E JR LOVEJOY F W JR. and YU P N Clinical and hemodynamic studies of myocardial fibrosis *Circulation 16* 332 1957

HYPERKINETIC STATES

BISHOP J M DONALD K W and WADE O L. Circulatory dynamics at rest and on exercise in the hyperkinetic states *Clin Sc 14* 329 1955

CASE R B BERGLUND E and SARNOFF S J Ventricular function VII Changes in coronary resistance and ventricular function resulting from acutely induced anemia and the effect thereon of coronary stenosis *Am J Med 18* 397 1955

EPSTEIN F H POST R S and MCDOWELL M The effect of an arteriovenous fistula on renal hemodynamics and electrolyte excretion *J Clin Invest 32* 233 1953

FERGUSON T B GREGG D E and SHADLE O Effect of blood and saline infusion on cardiac performance in normal dogs and dogs with arteriovenous fistulae *Circulation Res 2* 565 1954

FRANK, C W WANG H LAMMERANT J MILLER R and WÉGRIA R An experimental study of the immediate hemodynamic adjustments of acute arteriovenous fistulae of various sizes *J Clin Invest 34* 722 1955

GRAETTINGER J S MUENSTER J J CHECCHIA C S GRISSOM R L and CAMPBELL J A A correlation of clinical and hemodynamic studies in patients with hypothyroidism *J Clin Invest 37* 502 1958

HOLMGREN A *et al* Low physical working capacity in suspected heart cases due to inadequate adjustment of peripheral blood flow (vasoregulatory asthenia) *Acta med scandinav 158* 413 1957

LAHEY W J ARST D B SILVER M KLEEMAN C R and KUNKEL P Physiologic observations on a case of beriberi heart disease with a note on the acute effects of thiamine *Am J Med 14* 248 1953

LEIGHT L SNITER T H CLIFFORD G O and HELLEMS H K Hemodynamic studies in sickle cell anemia *Circulation 10* 653 1954

NICKERSON J L ELKIN D C and WARREN J V The effect of temporary occlusion of arteriovenous fistulae on heart rate stroke volume and cardiac output. *J Clin Invest 30* 215 1951

SHADLE O W FERGUSON T B SABISTON D C JR and GREGG D E The hemodynamic response to Lanatoside C of dogs with experimental aortic caval fistulae *J Clin Invest 36* 335 1957

for differentiation of mitral stenosis and regurgitation *Am J Cardiol 2* 24 1958
McDonald L Dealy J B, Jr Rabinowitz M and Dexter L Clinical physiological and pathological findings in mitral stenosis and regurgitation *Medicine 36* 237 1957
Riley R L *et al* Diffusing capacity of the lungs in patients with mitral stenosis studied postoperatively *J Clin Invest 35* 1008 1956
Ross J Jr Braunwald E and Morrow A G Clinical and hemodynamic observations in pure mitral insufficiency *Am J Cardiol 2* 11, 1958
Wade O L., Bishop J M, and Donald K W The effect of mitral valvotomy on cardiorespiratory function *Clin Sc 13* 511 1954
Williams M H Jr Pulmonary function studies in mitral stenosis before and after commissurotomy *J Clin Invest 32* 1094 1953
Wood J A Alexander J K Frank C W West J R and Richards D W Some clinical and physiologic effects of mitral commissurotomy *Circulation 13* 178, 1956

DISEASE OF THE AORTIC VALVE

Goldberg H Smith R C and Raber G Estimation of severity of aortic stenosis by combined heart catheterization *Am J Med 24* 853 1958
Gorlin R McMillan I K R Medd W E ,Matthews M B and Daley R Dynamics of the circulation in aortic valvular disease *Am J Med 18* 855 1955
McKusick V A Hahn D P Brayshaw J R and Humphries J O Some hemodynamic effects of the Hufnagel operation for aortic regurgitation studies in models and patients *Bull Johns Hopkins Hosp 95* 322 1954
Raber G and Goldberg H Left ventricular central aortic and peripheral pressure pulses in aortic stenosis *Am J Cardiol 1* 572 1958

DISEASE OF THE TRICUSPID VALVE

Killip, T III and Lukas D S Tricuspid stenosis *Am J Med 24* 836 1958

ISCHEMIC HEART DISEASE

Eckstein R W Effect of exercise and coronary artery narrowing on coronary collateral circulation *Circulation Res 5* 230 1957
Lee G de J Total and peripheral blood flow in acute myocardial infarction *Brit Heart J 19* 117 1957
Paul, M H Norman L R Zoll P M and Blumgart H L Stimulation of interarterial coronary anastamoses by experimental acute coronary occlusion *Circulation 16* 608 1957

HYPERTENSIVE HEART DISEASE

Freis E D *et al* The hemodynamic effects of hypertensive drugs in man III Hexamethonium *J Clin Invest 32* 1285 1953

GREEN H D Pharmacology of antihypertensive drugs *Am J Med 17* 70 1954

SMITH J R and HOOBLER S W Acute and chronic cardiovascular effects of pentolinium in hypertensive patients *Circulation 14* 1061 1956

TAYLOR S H DONALD K W and BISHOP J M Circulatory studies in hypertensive patients at rest and during exercise *Clin Sc 16* 351 1957

WIGGERS C J Dynamics of hypertension *Am Heart J 16* 516 1938

CONSTRICTIVE PERICARDITIS

BURWELL C S Constrictive pericarditis *Circulation 15* 161 1957

NYE R E JR LOVEJOY F W JR and YU P N Clinical and hemodynamic studies of myocardial fibrosis *Circulation 16* 332 1957

HYPERKINETIC STATES

BISHOP J M DONALD K W and WADE O L Circulatory dynamics at rest and on exercise in the hyperkinetic states *Clin Sc 14* 329 1955

CASE R B BERGLUND E and SARNOFF S J Ventricular function VII Changes in coronary resistance and ventricular function resulting from acutely induced anemia and the effect thereon of coronary stenosis *Am J Med 18* 397 1955

EPSTEIN F H POST R S and McDOWELL M The effect of an arterio venous fistula on renal hemodynamics and electrolyte excretion *J Clin Invest 32* 233 1953

FERGUSON T B GREGG D E and SHADLE O Effect of blood and saline infusion on cardiac performance in normal dogs and dogs with arteriovenous fistulae *Circulation Res 2* 565 1954

FRANK, C W WANG H LAMMERANT J MILLER R and WÉGRIA R An experimental study of the immediate hemodynamic adjustments of acute arteriovenous fistulae of various sizes *J Clin Invest 34* 722 1955

GRAETTINGER J S MUENSTER J J CHECCHIA C S GRISSOM R L and CAMPBELL J A A correlation of clinical and hemodynamic studies in pa tients with hypothyroidism *J Clin Invest 37* 502 1958

HOLMGREN A *et al* Low physical working capacity in suspected heart cases due to inadequate adjustment of peripheral blood flow (vasoregulatory asthenia) *Acta med scandinav 158* 413 1957

LAHEY W J ARST D B SILVER, M KLEEMAN C R and KUNKEL P Physiologic observations on a case of beriberi heart disease with a note on the acute effects of thiamine *Am J Med 14* 248 1953

LEIGHT L SNITER T H CLIFFORD G O and HELLEMS H K Hemody namic studies in sickle cell anemia *Circulation 10* 653 1954

NICKERSON J L ELKIN D C and WARREN J V The effect of temporary occlusion of arteriovenous fistulae on heart rate stroke volume and cardiac output *J Clin Invest 30* 215 1951

SHADLE O W FERGUSON T B SABISTON D C JR and GREGG D E The hemodynamic response to Lanatoside C of dogs with experimental aortic caval fistulae *J Clin Invest 36* 335 1957

CHAPTER 6

DISEASES OF LUNG AIRWAYS

Bronchial asthma, chronic obstructive emphysema and bronchiectasis will be discussed as diseases of the lung airways Although each disease may be accompanied by other parenchymal alterations the primary lesion in all three conditions is probably in the tracheobronchial tree The interrelationships between the three conditions are complex and not totally defined Emphysema may complicate both of the other two disorders Chronic bronchitis another disorder of the airways and also a possible precursor of emphysema, has received too little attention from the physiological standpoint to warrant extensive discussion It will be mentioned in relationship to emphysema

BRONCHIAL ASTHMA

PATHOPHYSIOLOGY

Acute

Bronchial asthma is characterized by attacks of airway obstruction These are due to bronchospasm edema of the bronchial mucosa and hypersecretion into the bronchi During the acute attack spirometric study reveals expiratory delay and usually reduced vital capacity In severe cases the airway obstruction leads to hypoxemia and carbon dioxide retention The residual volume of the lung is increased, because the narrowed airways prevent deep expiration Marked impairment of mixing of inspired air within the lung may also be present All of these abnormalities are present in emphysema However they are reversible in asthma in contradistinction to the permanent impairment found in emphysema In addition the diffusing capacity of the lung is not reduced in uncomplicated asthma no matter how severe the airway obstruction A low diffusing capacity is characteristic of emphysema

Chronic

Between attacks the asthmatic patient may be perfectly well with out any abnormality of pulmonary function or a variable degree of bronchospasm may persist The latter causes expiratory delay on spirometry increase of the residual volume of the lung poor mixing of gases in the lung and hypoxemia This situation may be difficult to distinguish from chronic pulmonary emphysema However, in asthma there is marked variability in the degree of physiological im pairment from time to time more relief of the airway obstruction from bronchodilators than is seen in emphysema and a relatively nor mal diffusing capacity of the lungs Measurement of the diffusing capacity appears to offer the best single means of differentiating asthma from emphysema

The physiological distinction between asthma and emphysema is highlighted by the data in Table 2 The patients with asthma all ex hibit marked variability of airway obstruction as indicated by the wide range of values for miximal mid-expiratory flow rate (M M F) a variable degree of hypoxemia and CO_2 retention and a relatively high diffusing capacity They have pulmonary hypertension which is accentuated by exercise but which is not quite as severe as in emphy sema

Physiological study is useful in evaluating the severity of bronchial asthma and in differentiating between asthma and emphysema In addition the efficacy of various bronchodilators is readily evaluated in the individual patient by spirometric study before and after admin istration of the drugs

COMPLICATIONS

That asthma eventually leads to emphysema is a matter of some debate Asthma is primarily a disease of women and children whereas emphysema is most commonly found in older men Patients with emphysema do not usually give a history of bronchial asthma and many patients with longstanding asthma do not have the reduction of the diffusing capacity or the permanent airway obstruction character istic of emphysema It is likely that the two are separate disorders although asthma may become chronic and just as disabling as ob structive emphysema

Death from bronchial asthma is unusual It results from severe airway obstruction associated with inspissation of thick mucoid plugs

TABLE 2 RESULTS OF CARDIOPULMONARY FUNCTION STUDIES IN 22 PATIENTS WITH EMPHYSEMA AND 11 PATIENTS WITH ASTHMA

Test	Normal	Asthma Mean	Asthma Range	Asthma N	Emphysema Mean	Emphysema Range	Emphysema N
M M F							
l /sec	3 5	1 01	27–1 87	11	40	23– 89	22
Total range			20–3 30	106[b]		16–1 00	280[b]
Vital cap —% normal	90–110	67	32–87	11	53	38–76	22
Art O_2 Sat —%							
Rest	97–99	90	84–97	11	86	76–93	22
Exercise	97–99	91	83–98	10	83	69–92	19
Art P_{CO_2}—mm Hg							
Rest	40	44	29–70	11	50	35–72	22
Exercise	40	43	29–47	10	51	37–63	19
Res vol /total lung cap —%	<30				66	55–78	16
7 nitrogen—%	<2				5	2–10	16
Dead space/tidal vol							
Rest	<30	38	21–55	10	48	37–69	21
Exercise	<30	35	23–53		45	33–63	18
CO diff cap —cc /min /mm Hg							
Rest	15	16 0	11 4–26 3	11	6 3	3 4–12 6	22
Exercise	25	20 2	13 0–39 6		9 4	6 5–12 7	17
Cardiac index—liters/min /sq M							
Rest	3 0	3 80	1 99–5 31	5	3 21	2 03–4 60	18
Exercise	4 0	5 10	4 03–6 65		4 35	2 70–5 17	14
Pulm art pr —mm Hg							
Rest	22/8	26/9 (18)	15–32/6–12	5	36/16 (25)	19–63/5–34	17
Exercise	30/15	50/23 (34)	32–69/12–35	5	54/25 (38)	19–89/5–41	14

The average data are listed In each case the mean of 1 or more measurements on each patient was used to obtain the group mean N refers to the number of patients studied for that particular measurement Maximal mid-expiratory flow rate (M M F) and vital capacity were calculated from the spirogram In the case of the former the total range and total number of measurements are listed as well as the range of mean values for each patient Lung volumes and 7 minute residual nitrogen were obtained by the open circuit nitrogen-dilution technique Dead space was calculated from the Bohr equation with the use of the arterial P_{CO_2} as representative of the alveolar P_{CO_2} Diffusing capacity for carbon monoxide (D_{CO}) was measured by the steady state method of Filley *et al* Cardiac index was calculated by the Fick formula with the use of data obtained at cardiac catheterization with simultaneous measurement of the pulmonary artery pressure The average mean pulmonary artery pressure for each group is listed in parentheses next to the average instantaneous pressure

[b] Total number of measurements

in the small airways Expectorants such as potassium iodide may be of value if given early

Right heart failure a serious complication of emphysema, is un usual in asthma Its infrequency, reflected in the fact that pulmonary hypertension is less common in asthma than in emphysema may be due to the fact that alveolar capillary tissue is not destroyed in asthma This is manifest in the relatively normal diffusing capacity As in emphysema hypoxemia may develop and initiate the chain of events which leads to right heart failure But the relatively intact pul monary vascular bed makes this complication quite rare

TREATMENT

The most effective form of therapy for acute bronchial asthma is the administration of a bronchodilator Intravenous or subcutaneous injection of epinephrine rectal or intravenous administration of aminophylline or nebulization with isoproterenol or other broncho dilators is generally followed by prompt symptomatic improvement, reflected in increased speed of expiration on spirometry In severe at tacks nebulized bronchodilators may be of little value because the medication does not get down into the areas of bronchospasm Under these circumstances administration of the drug by inspiratory posi tive pressure may give prompt relief Large doses of steroids will gen erally terminate an acute attack of asthma within 48 hours

Therapy of chronic asthma involves elimination of agents that pro voke bronchospasm and the use of bronchodilators Steroids may be used in refractory cases Vagotomy has been recommended by some but asthma can generally be controlled by medical threapy and sur gery is rarely necessary

CHRONIC OBSTRUCTIVE EMPHYSEMA

PATHOGENESIS

Obstruction of the small airways is probably the primary lesion in chronic obstructive emphysema Fragmentation and rupture of the alveoli are also present The interrelationship between these two processes the airway obstruction and the parenchymal destruction is not entirely clear Some feel that airway obstruction causes parenchy mal destruction some hold the opposite view and others feel that the two are unrelated Against the first possibility is the fact that chronic

asthma is not necessarily followed by the development of emphysema However the bronchiolar disease which causes emphysema is different from the spasm of large airways characteristic of asthma In support of the second hypothesis Dayman has pointed out that loss of lung parenchyma deprives the airways of the elastic support which helps to hold them open This causes the airways to collapse during expiration when the positive pressure in the chest is unopposed by the retractive forces of normal lung parenchyma Although this mechanism is undoubtedly of importance in increasing the airway obstruction in pulmonary emphysema, the primary abnormality probably lies in the airways

Recent pathological studies have suggested that the primary abnormality in emphysema lies in the small airways or bronchioles Although obstruction of large airways does not lead to fragmentation and rupture of alveoli alveolar destruction is generally found in areas in which there is also evidence of bronchiolitis McLean has suggested that bronchiolitis leads to obstruction or dilatation and eventually to disappearance of these small airways The alveoli distal to the occluded or absent bronchioles become ventilated by collateral channels through the pores of Cohn This process is more effective during inspiration than during expiration and so air enters but fails to leave the alveoli which as a result become dilated and eventually rupture perhaps during a cough This concept is particularly interesting in connection with the apparent clinical association between chronic bronchitis and emphysema According to McLean s observations obstruction of the small airways with mucous plugs is a common accompaniment of the frequent respiratory infections which plague most people Normal individuals can expel these plugs by coughing and thus prevent secondary emphysema Patients with chronic bronchitis may have lost the cleansing ciliary action of the bronchial mucosa and may be particularly prone to develop frequent and irreversible bronchiolar obstruction On the other hand there is some evidence suggesting that patients with chronic bronchitis who have shortness of breath because of chronic airway obstruction do not have the reduced diffusing capacity characteristic of emphysema whereas patients with similar shortness of breath and airway obstruction who do have a low diffusing capacity do not give a history of chronic bronchitis It is possible that true emphysema follows a generalized severe bronchiolitis perhaps apparent clinically only

as a cold or the flu whereas chronic bronchitis even when associated with airway obstruction and dyspnea does not necessarily lead to emphysema Although the weight of evidence favors the hypothesis that emphysema is related to bronchiolar pathology its relation to bronchitis is not clear and convincing exposition of the pathogenesis of the disorder awaits the results of sequential physiologic studies on patient from early until late in the development of the disease

PATHOPHYSIOLOGY

Airway Obstruction

The pathophysiology of pulmonary emphysema follows from the two basic abnormalities the persistent airway obstruction and the loss of lung parenchyma Obstruction of the small airways makes it difficult to move air in and out of the lung This is reflected in a slow rate of airflow on spirometry particularly during expiration During a forced expiration the expiratory impediment becomes more severe as the patient blows more and more air out of his lungs As the lung gets smaller the obstruction to expiration increases This causes reduction of the maximal mid expiratory flow rate (M M F) and of the timed vital capacity and also explains why the lungs are overinflated in emphysema It is easier for the patient to breathe with his lungs inflated than collapsed

The work of breathing is so great in emphysema that patients choose a level of alveolar ventilation which is subnormal relative to their metabolic needs They prefer not to do the large amount of work that would be necessary if they were to move normal amounts of air in and out of their alveoli The result is elevation of the alveolar carbon dioxide tension and reduction of the alveolar oxygen tension This is one cause of the hypoxemia and CO_2 retention characteristic of emphysema Dyspnea the outstanding symptom of emphysema is also related to the increased work of breathing (Chap 12)

Loss of Lung Parenchyma

Loss of lung parenchyma is reflected in reduction of the diffusing capacity of the lung and in increased pulmonary vascular resistance The diffusing capacity is a reflection of the number of alveolar capillaries present in the lung and it is reduced when the alveoli become fragmented and destroyed Although impaired diffusion may

accentuate the hypoxemia it is of slight consequence in other respects

Destruction of alveoli is also associated with destruction of small pulmonary blood vessels This causes increased pulmonary vascular resistance, the main cause of pulmonary hypertension in emphysema The pulmonary artery pressure is only slightly elevated at rest, but it increases markedly during exercise As pointed out in Chapter 2, a marked reduction of pulmonary vascular resistance may be associated with only slight pulmonary hypertension when the cardiac output is normal However, exercise leads to a marked increase of the pulmonary artery pressure when increased amounts of blood pass through the restricted inexpansile vascular bed

Hypoxemia and Carbon Dioxide Retention

As mentioned above, one cause of hypoxemia and CO_2 retention in emphysema is reduction of alveolar ventilation The hypoxemia is accentuated by the impaired diffusion The third cause of arterial blood gas abnormality is the most important poor mixing of blood and gas in the lung Because of the variability of the degree of airway obstruction and of the loss of lung elasticity from place to place in the lung some areas are ventilated quite well whereas other areas are not ventilated at all In addition, the degree of loss of pulmonary capillaries varies from place to place in the lung Thus some alveoli receive large amounts of blood and others receive very little Since the areas that are hyperventilated are not necessarily those that are overperfused and since the hypoventilated areas are not necessarily underperfused, there is marked variability of the ventilation perfusion ratios in various parts of the lung Some alveoli have a high oxygen content whereas others have a very low oxygen content This is the major cause of hypoxemia in pulmonary emphysema (Chap 11)

Increased Residual Volume

As mentioned above it is easier for patients with emphysema to breathe with their lungs inflated than in the normal partially collapsed position That is why they have chronic overinflation of their lungs and the volume of air left in the lungs at the end of a normal expiration the functional residual capacity is increased

In addition it is impossible for these patients to empty their lungs normally with forced expiration Airway obstruction becomes worse

as the patient breathes out It eventually becomes complete As a result the volume of air left in the lung at the end of a maximal expiration the residual volume, is far in excess of the normal 25 to 40 per cent of the total lung capacity

The increase of these components of lung volume (functional residual capacity and residual volume) is a distinctive feature of pulmonary emphysema but by itself is of little functional consequence The symptoms and physiological abnormalities of emphysema are not related to these physical characteristics of the disease However the increased residual volume is associated with impaired mixing of inspired gas within the lung This leads to uneven alveolar ventilation which as mentioned is a major cause of hypoxemia But the magnitude of the lung volume per se bears no relationship to arterial blood gas composition (Chap 1)

Table 2 shows the average values for some aspects of pulmonary function in emphysema In general there is homogeneity among these patients in respect to their pulmonary function They all have a similar degree of severe intractable airway obstruction, as reflected in the low M M F They have moderate hypoxemia and CO_2 retention a low diffusing capacity a large residual volume of the lung and pulmonary hypertension which is moderate at rest but quite severe during exercise

COMPLICATIONS

These patients may continue in a state of severe physiological impairment for many years Figure 17 shows the sequential data obtained on one patient with emphysema Over a 2½ year period there was little progression of disordered pulmonary function Indeed there was little variation of ventilatory function from month to month This state of chronic disability is apt to be punctuated by episodes of acute respiratory distress usually the result of infection which cause temporary increase in the functional abnormalities These should be treated promptly and vigorously

Right Heart Failure

A serious but reversible complication of emphysema is right heart failure This is causally related to hypoxemia and is always associated with a very low arterial oxygen saturation and marked CO_2 retention Pulmonary vascular resistance already high because of destruction

of arterioles in the lung, is increased by hypoxemia This may be due to a direct effect of hypoxia on the pulmonary arterioles It is also due to the secondary polycythemia which increases resistance by increasing the viscosity of the blood In addition hypoxemia causes an increase of the cardiac output This adjustment is necessary if the tissues are to receive adequate amounts of oxygen in the face of a

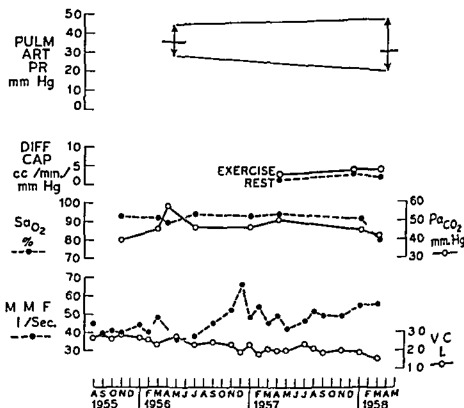


Fig 17 Sequential data o pulmonary artery p s e diffusing capac ty a te al blood gases and vent latory funct on in a typ cal pat ent with obstruct e emphysema Over a three year period the only ev dence of prog essive funct o al impairment was slight reduction of the v tal capac ty (V C)

reduced arterial oxygen saturation *All* these factors contribute to the development of severe pulmonary hypertension which places an increased work load on the right ventricle This is met by elevation of the end diastolic pressure in the right ventricle (Chap 4), which leads to venous hypertension and eventually to salt and water retention

Patients with right heart failure due to emphysema usually respond

very well to treatment Digitalis may cause an increase of the cardiac output even if it is high before treatment, and reduction of the venous pressure An even more important aspect of therapy is elimination of the hypoxemia by overcoming the underlying airway obstruction with bronchodilators and antibiotics Oxygen may be given carefully preferably in combination with inspiratory positive pressure so as not to induce respiratory depression (Chap 10) Phlebotomy is indicated when polycythemia is present in order to reduce the viscosity of the blood and hence the pulmonary vascular resistance Finally, diuretics are used as in any type of congestive heart failure

So far the phrase cor pulmonale has not been used Cor pulmonale is defined as dilatation hypertrophy or failure of the right ventricle because of chronic pulmonary disease The term is of very little clinical value A patient with emphysema has cor pulmonale when the right ventricle becomes hypertrophied But this may not be obvious clinically and is indeed of little clinical consequence On the other hand the degree of pulmonary hypertension and the presence or absence of signs of right heart failure are of clinical importance The term cor pulmonale should be reserved for use by the pathologist being used by the clinician only as a reflection of his anticipation of a postmortem finding Terms such as right ventricular failure the congested state and pulmonary hypertension are much more meaningful in the clinical assessment of the effect of pulmonary disease on cardiac function

Alveolar Hypoventilation

Another complication is alveolar hypoventilation Chronic alveolar hypoventilation is more or less the rule in emphysema A mild degree is usually of no great consequence to the patient and can be well tolerated for long periods of time The hypoventilation is due to an increased dead space so that less of the tidal volume reaches the alveoli and to the fact that the patient with emphysema has to do excessive work to move air in and out through the narrow airways He chooses a subnormal level of alveolar ventilation rather than do the large amount of extra respiratory work which would be required to maintain a normal alveolar carbon dioxide tension In addition an increase of the alveolar ventilation requires so much work from the respiratory muscles that the resultant increase of CO production may more than outweigh the increased alveolar ventilation Hyper

ventilation may actually cause elevation of the alveolar carbon dioxide tension

Alveolar ventilation becomes further reduced in acute respiratory insufficiency associated with infections The resultant CO_2 retention may lead to lethargy and to depression of the respiratory center with even further depression of ventilation This is particularly true if the accompanying hypoxemia a major stimulus to respiration is eliminated by having the patient breathe oxygen The most beneficial treatment of this condition allows an increase of the alveolar ventilation This is achieved by improvement of the underlying airway obstruction and by mechanical ventilatory aids The former involves bronchodilators in order to reduce bronchospasm, antibiotics in order to reduce inflammation of the bronchial mucosa and coughing to remove airway obstructing secretions Severe cases may require bronchoscopy and/or tracheal aspiration Mechanical aids include inspiratory positive pressure (IPPB) to assist the patient to inspire deeply and in advanced cases of ventilatory insufficiency a respirator The latter is usually not necessary since satisfactory improvement generally follows the use of bed rest, bronchodilators IPPB and antibiotics On the other hand, one should not hesitate to use a respirator when a patient with alveolar ventilatory insufficiency is comatose

TREATMENT

Management of the patient with chronic pulmonary emphysema centers about bronchodilators prompt treatment of upper respiratory infections and avoidance of inhalation of substances which irritate the tracheobronchial tree Cigarette smoking has been shown to increase the airway obstruction in patients with emphysema although normal subjects are not affected With these measures some symptomatic improvement usually occurs and progression of the disease may be prevented

A number of other therapeutic measures have been advocated for restoration of the impaired pulmonary function toward normal Most of these have proved to be disappointing but some of them will be discussed briefly

The benefit ascribed to pneumoperitoneum is based on the notion that elevation of the diaphragm to its normal position should restore its mechanical efficiency Contraction of the low diaphragm of the

patient with emphysema may decrease rather than increase the size of the thoracic cavity Restoration of the diaphragm to a higher position might restore its effectiveness Indeed, pneumoperitoneum is usually followed by improvement of diaphragmatic function on fluoroscopy, improved mixing of gases in the lung and improved arterial blood gas composition but symptomatic improvement is often lacking Despite its inconvenience pneumoperitoneum is worth a trial in the disabled patient

There is a sound rationale for the use of breathing exercises in emphysema Symptomatic improvement may follow their use They have three major purposes (1) training of the abdominal muscles to force the diaphragm up during expiration and down during inspiration (2) relaxed expiration to minimize the expiratory obstruction induced by forceful expiration and (3) prolonged expiration to empty the lungs as much as possible In addition enthusiastic urging of a therapeutic measure which requires the patient s time and effort has desirable psychological effects For details about the techniques of breathing exercises and of ancillary ventilatory aids the reader should consult the publications of Barach and of Miller

Except for excision of bullae which are actually compromising function by pressure on adjacent lung surgery has little if anything to offer the patient with emphysema The concept that one can with benefit safely excise inactive areas of diffuse emphysematous change appears to require more confirmation by definitive studies Recently interest has been aroused in tracheostomy, or a tracheal fenestration operation to promote aspiration of secretions from deep within the airways Such treatment has not received adequate physiologic evaluation at this time

As in most types of chronic disease the patient with emphysema eagerly desires improvement and is apt to feel better after each new form of therapy The physician must evaluate each new therapeutic measure with caution Demonstrable improvement of pulmonary function should be a prerequisite to the general adoption of any new therapeutic measure particularly if it involves risk to the patient

BRONCHIECTASIS

Bronchiectasis stands in distinct contrast to asthma and emphysema in that extensive abnormalities are often associated with little disorder of pulmonary function Considerable function may remain

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EMPHYSEMA

BALDWIN E DE F COURNAND A and RICHARDS D W JR Pulmonary insufficiency III A study of 122 cases of chronic pulmonary emphysema *Medicine 28* 201 1949

BARACH A L Restoration of diaphragmatic function by breathing exercises in pulmonary emphysema *New York State J Med 56* 3319 1956

BARACH A L and BICKERMAN H A Eds *Pulmonary emphysema* Baltimore Williams & Wilkins 1956

BATES D V KNOTT J M S and CHRISTIE R V Respiratory function in emphysema in relation to prognosis *Quart J Med 25* 137 1956

BECKLAKE M R GOLDMAN H I and MCGREGOR M The effects of pneumoperitoneum on lung function in pulmonary emphysema *Thorax 9* 222 1954

BLAIR E and HICKAM J B Quantitative study of intrapulmonary gas mixing in emphysema *Am J Med 18* 519 1955

BORDEN C W WILSON R H EBERT R V and WELLS H S Pulmonary hypertension in chronic pulmonary emphysema *Am J Med 8* 701 1950

BOUTOURLINE YOUNG H J and WHITTENBERGER J L The use of artificial respiration in pulmonary emphysema accompanied by high carbon dioxide levels *J Clin Invest 30* 838 1951

CHERNIACK R M The physical properties of the lung in chronic obstructive pulmonary emphysema *J Clin Invest 35* 394 1956

CHRISTIE R V Elastic properties of the emphysematous lungs and their clinical significance *J Clin Invest 13* 295 1934

COHN J E CARROLL D G and RILEY R L Respiratory acidosis in patients with emphysema *Am J Med 17* 447 1954

DAYMAN H Mechanics of airflow in health and in emphysema *J Clin Invest 30* 1175 1951

EBERT R V Pulmonary emphysema *Ann Rev Med 7* 123 1956

EICH R H GILBERT R and AUCHINCLOSS H J JR The acute effects of smoking on the mechanics of respiration in chronic obstructive pulmonary emphysema *Am Rev Tuberc & Pulmonary Diseases 76* 22 1957

FERRER M I *et al* Some effects of digoxin upon the heart and circulation in man *Circulation 1* 161 1950

FERRER M I and HARVEY R M Management of cor pulmonale *New York State J Med 57* 2489 1957

FRY D L EBERT R V STEAD W W and BROWN C C The mechanics of pulmonary ventilation in normal subjects and in patients with emphysema *Am J Med 16* 80 1954

HARVEY R M FERRER M I RICHARDS D W JR and COURNAND A Influence of chronic pulmonary disease on the heart and circulation *Am J Med 10* 719 1954

KORY R C ROEHM D C MENEELY G R and GOODWIN R A JR Pulmonary function and circulatory dynamics in artificial pneumoperitoneum Studies on patients with pneumoperitoneum as a therapeutic measure in pulmonary emphysema *Dis Chest 23* 608 1953

even in areas of lung involved by extensive bronchiectasis Dilatation of the larger airways need not affect the ventilation and perfusion of the alveoli the important factors in pulmonary function In addition expansion of the collateral circulation to bronchiectatic areas prevents hypoxemia (Chap 8) Functional limitation only occurs if the disease is extensive and associated with pulmonary emphysema or with diffuse bronchospasm

Bronchiectasis poses a problem because of repeated infection and hemoptysis clear cut indications for surgery It should be borne in mind that resection of a bronchiectatic segment will in most instances deprive the patient of some functioning lung On the other hand resectional surgery is well tolerated in this disease because the function of the remaining lung tissue is generally normal

In connection with the radiographic diagnosis of bronchiectasis the studies of Black and Roos are of interest These workers have shown that the administration of Lipiodol for bronchographic study has no deleterious effect on respiratory gas exchange Thus the presence of pulmonary emphysema or of other types of respiratory insufficiency need not be a deterrent to the performance of bronchography

REFERENCES

ASTHMA

ABBOTT O A VAN FLEIT W E ROBERTO A E and SALOMONE F P Studies on the function of the human vagus nerve in various types of intra thoracic disease *J Thoracic Surg 30* 564 1955

BATES D V Impairment of respiratory function in bronchial asthma *Clin Sc 11* 203 1952

CAMPBELL E J M MARTIN H B and RILEY R L Mechanisms of airway obstruction *Bull Johns Hopkins Hosp 101* 329 1957

DIMITROV SZOKODI D HUSVÉTI A and BALOGH G Lung denervation in the therapy of intractable bronchial asthma *J Thoracic Surg 33* 166 1957

FYLES T W PARE J A P and ROSS B The effect of corticotropin and cortisone on respiratory function in bronchial asthma *J Allergy 26* 340 1955

GELFAND M L Chronic cor pulmonale in long standing bronchial asthma *Am J Med 10* 27 1951

HERSCHFUS J A BRESNICK E and SEGAL M S Pulmonary function studies in bronchial asthma *Am J Med 14* 25 1953

MCILROY M B ELDRIDGE F L and MARSHALL R The mechanical properties of the lungs in asthma *Clin Sc 15* 345 1956

CHAPTER 7

DISEASES OF THE LUNG PARENCHYMA AND CHEST WALL

PULMONARY FIBROSIS

Roentgenographic vs. Functional Effects

Pulmonary fibrosis has many different causes, varies in extent and location and produces a variety of types and degrees of abnormality of pulmonary function. Some types of fibrosis may appear as conglomerate densities throughout both lungs on x ray and yet may cause little interference with pulmonary function because many areas of pulmonary tissue are not involved by the pathological process. On the other hand, diffuse fibrosis of the alveolar walls, which may result from the inhalation of beryllium or from irradiation, sarcoidosis alveolar cell carcinoma (adenomatosis) or unknown causes such as the Hamman Rich syndrome may be associated with little abnormality on x ray but with profound impairment of diffusion across the alveolar walls the syndrome of alveolar-capillary block. If each alveolar wall is thickened to three times its normal diameter the resultant impairment of diffusion is much greater than if one of three alveoli is completely obliterated by fibrous tissue Elimination of one third of the lung if the remaining tissue is normal, can be well tolerated whereas generalized involvement, albeit less obvious in any one place is more serious

Hyperventilation and Impaired Diffusion

Diffuse fibrosis of the alveolar walls regardless of etiology may cause very little impairment of ventilatory function but hyperventilation and impaired diffusion of oxygen are generally present The

McLean K H The pathogenesis of pulmonary emphysema *Am J Med 25* 62 1958

Mead J Lindgren I and Gaensler E A The mechanical properties of the lungs in emphysema *J Clin Invest 34* 1005 1955

Miller W F A physiologic evaluation of the effects of diaphragmatic breathing training in patients with chronic pulmonary emphysema *Am J Med 17* 471 1954

Miller W F Physical therapeutic measures in the treatment of chronic bronchopulmonary disorders *Am J Med 24* 929 1958

Riley R L The work of breathing and its relation to respiratory acidosis. *Ann Int Med 41* 172 1954

Segal M S and Dulfano M J *Chronic Pulmonary Emphysema* New York Grune & Stratton 1952

Shepard R H *et al* The maximal diffusing capacity of the lung in chronic obstructive disease of the airways *Am Rev Tuberc & Pulmonary Diseases 71* 249 1955

Stone D J Schwartz A Newman W Feltman J A and Lovelock F J Precipitation by pulmonary infection of acute anoxia cardiac failure and respiratory acidosis in chronic pulmonary disease *Am J Med 14* 14 1953

Tenney S M Respiratory control in chronic pulmonary emphysema. A compromise adaptation *J Maine Med A 48* 375 1957

West J R Baldwin E de F Cournand A and Richards D W Jr. Physiopathologic aspects of chronic pulmonary emphysema. *Am J Med 10* 481 1951

Williams M H Jr and Zohman L R Cardiopulmonary function in chronic obstructive emphysema *Am Rev Resp Dis 80* 710 1959

Wright G W Place R and Princi F Physiological effects of pneumoperitoneum upon the respiratory apparatus *Am Rev Tuberc 60* 706 1949

BRONCHIECTASIS

Black H and Roos A The effect of Lipiodol on alveolar gas exchange *J Clin Invest 30* 338 1951

Long J H Norris C M Burnett W E and Wester M S Bronchospirometric studies in bronchiectasis before and after lobectomy *J Thoracic Surg 19* 477 1950

Smith G A Siebens A A and Storey C F Preoperative and postoperative cardiopulmonary function studies in patients with bronchiectasis *Am Rev Tuberc 69* 869 1954

Vosti K L. Pearson J Saxton G Lepper M and Dowling H F Pulmonary function in bronchiectasis *Clin Res 5* 228 1957





Fg 18 Chest x ray of a pat ent w th ext n e fb o d t s r o do (A) who t ally d elop d

hyperventilation, which is probably of reflex origin causes reduced arterial carbon dioxide tension both at rest and during exercise Dyspnea is common in these patients and probably is the result of the hyperventilation plus reduction of lung compliance (Chap 12) The impaired diffusion may not be severe enough to cause hypoxemia, since the diffusing capacity must be greatly reduced before the arterial oxygen saturation falls significantly (Chap 11) However if hypoxemia is present, it is greatly increased by exercise and completely relieved, even during exercise by oxygen breathing

Although one may suspect diffuse pulmonary fibrosis as the cause of dyspnea on the basis of hyperventilation and diffuse x ray changes, definitive diagnosis requires measurement of the diffusing capacity of the lungs There is a fairly good correlation between the severity of dyspnea and the degree of reduction of the diffusing capacity and a normal diffusing capacity tends to exclude significant pulmonary fibrosis as a cause of shortness of breath Measurement of the diffusing capacity may prove to be of value in the assessment of pulmonary fibrosis due to industrial exposure to inhaled irritants

Ventilatory Function

As mentioned ventilatory function may be normal in pulmonary fibrosis but severe involvement leads to general reduction of lung volume of which the most easily measured subdivision is the vital capacity Vital capacity is reduced in direct proportion to the extent to which fibrous tissue replaces air containing spaces and prevents lung expansion The typical spirometric picture in pulmonary fibrosis is reduction of the vital capacity without expiratory delay The increased lung stiffness and replacement of air containing tissue by fibrous tissue does not lead to airway obstruction and so air may be moved rapidly in and out of the tracheobronchial tree The maximal breathing capacity may be relatively normal because the patient can breathe small volumes very rapidly Timed vital capacity and maximal mid expiratory flow rate (M M F) may also be relatively normal

Diffuse fibrotic involvement of the airways may cause airway obstruction but such is more often the result as in sarcoidosis of compression of the airways by enlarged lymph nodes Pulmonary fibrosis does not necessarily lead to emphysema and the common use of the diagnostic term fibrosis and emphysema" is to be deplored





Fg 18 Ch st x r y of a pat ent w th t sl e fib o s s d to sa co do s (A) who e entu lly de l p d a b lla n th l ft uppe lobe (B)

The two diseases may be associated, but they are very different physiologically and pathologically However, fibrotic occlusion of small airways may lead to emphysema Figure 18 represents the sequential development of a bulla in the left upper lobe of a patient with diffuse fibrosis due to sarcoid Rupture of the bulla and collapse of the lung was the eventual cause of death in this patient, who had lived with evidence of right heart failure and with a vital capacity of only 600 cc for more than two years

Pulmonary Hypertension

In addition to reduction of the diffusing capacity reflex tachypnea reduction of lung volume, and increased lung stiffness diffuse pulmonary fibrosis may cause reduction of the pulmonary vascular bed by destruction and narrowing of the pulmonary blood vessels This is a late development which leads to irreversible pulmonary hypertension and eventually right heart failure That this need not occur is evident from the data in Table 3 in which it may be seen that severe reduction of the diffusing capacity may be present without pulmonary hypertension even during exercise Apparently, fibrosis may involve the alveolar walls without compressing the blood vessels Reduction of the diffusing capacity precedes the development of pulmonary hypertension The reverse might be expected in primary disease of the lung blood vessels (Chap 8) The pulmonary hypertension in pulmonary fibrosis in contrast to that present in emphysema is relatively fixed and does not result from hypoxemia

SARCOIDOSIS

Hilar Adenopathy

Sarcoidosis may produce a variety of functional disturbances and the extent of physiological impairment is a guide to the need for steroid therapy The most common form of sarcoidosis hilar adenopathy is generally without functional effect and does not require therapy As mentioned above it may occasionally cause airway obstruction but spontaneous remission is the rule and there is some question as to whether or not steroids are of any value in this form of the disease

TABLE 3 RESULTS OF STUDIES OF CARDIOPULMONARY FUNCTION IN 7 CASES OF PULMONARY FIBROSIS STUDIED AT GRASSLANDS HOSPITAL

Patient	*Diagnosis*	*Rest or exercise*	*Art Blood*		*Diff cap cc CO/min (mm Hg)*	*Pulm art pressure (mm Hg)*	*Cardiac output (liters/min)*	*Vital cap (%)*	*M M F (liters/sec)*
			P_{CO_2} *(mm Hg)*	*So (%)*					
W B	Tbc	Rest	38	91	12 7	26/8	3 20	66	1 06
		Ex	39	87	13 2	32/10	9 12		
B M	Sarcoid	Rest	40	87	11 5	13/3	4 00	40	2 16
		Ex	37	84	10 8	14/6	5 58		
F G	Tbc	Rest	45	88	8 7	29/11	6 45	103	6 90
		Ex.	37	93	8 8	29/15	7 56		
C G	Sarcoid	Rest				35/15		74	2 23
		Ex			12 0	44/?			
M G	Sarcoid	Rest	55	91	10 0	52/18	4 71	37	1 33
		Ex	60	84	7 7	95/50	9 00		
M S	Sarcoid	Rest	41	78	3 9	66/?	6 50	79	1 61
		Ex	36	66	5 4	85/?	8 55		
P C	Idiopathic	Rest	45	80	5 4	34/?		53	2 40
		Ex	42	91	6 6	30/?	12 9		

The diffusing capacity is reduced in each case and there is a variable degree of pulmonary hypertension and of reduction of the vital capacity CO_2 retention is uncommon but hypoxemia exaggerated by exercise is often present

Alveolar Capillary Block

Diffuse pulmonary involvement with alveolar-capillary
be physiologically indistinguishable from the Hamman Ricl
and from pulmonary adenomatosis It is a definite ind
steroid therapy Cases have been reported—Figure 19 is a

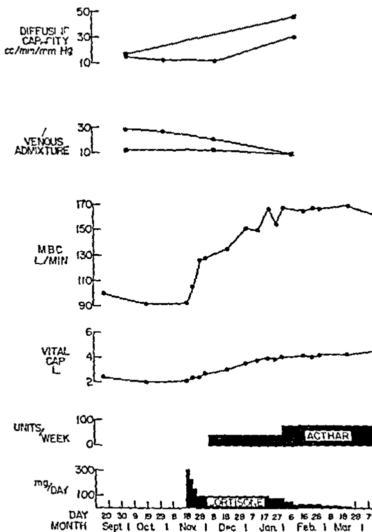


Fig 19 ...eral me surem nts of pulmonary funct on in a cas of d ff
... o do s treated w th st oids Note the r sto at on toward no mal of the d

—in which the ventilatory and diffusion abnormalities were completely reversed after the administration of steroids Since remissions may occur spontaneously it is not possible to be certain that steroids caused the improvement in these patients, but experience to date suggests that if given early in the course of the disease, steroids may materially improve pulmonary function If given later when the granulomatous pathologic changes have been replaced by fibrous tissue, improvement may be minimal or absent It is important to evaluate pulmonary function in patients suspected of having diffuse pulmonary involvement so that, if diffusion is impaired steroids may be given early when there is a chance of their being effective

Isolated Parenchymal Lesions

An uncommon form of sarcoidosis consists of conglomerate, diffuse snowball densities throughout both lung fields on x ray Such patients may have no symptoms and normal pulmonary function despite the presence of large lesions in each lung There is no need for steroids in patients of this type

TUBERCULOSIS

Effect on Pulmonary Function

Although ventilatory studies have been performed on large numbers of patients with pulmonary tuberculosis, the effects of this disease on other pulmonary functions and the modification of these effects by chemotherapy and by steroids, remain to be defined Localized disease is, from the functional standpoint of little consequence But the effect of extensive tuberculosis on pulmonary function is of great consequence Despite x ray and clinical remission, patients with such disease may develop crippling pulmonary fibrosis and/or emphysema It is important to learn whether or not these complications may be prevented by steroids

The mechanism of the development of emphysema is not clear It may occur in patients whose disease appears to be restricted to the upper lobes Yet upper lobe retraction should not of itself cause diffuse pulmonary emphysema It is possible that unsuspected extensive involvement of the small airways by the acute infection is responsible This picture may become clarified by long term studies of various

aspects of pulmonary function in patients with pulmonary tuberculosis

Oxygen and the Tubercle Bacillus

A different aspect of respiratory physiology has bearing on the pathogenesis and treatment of tuberculosis The tubercle bacillus requires oxygen for its growth and fails to survive in oxygen poor milieu Pulmonary tuberculosis is rare at high altitudes Also disease is apt to develop in areas of the lung that receive relatively more ventilation than perfusion with blood and hence contain a relatively high oxygen tension e g the upper lobes of the human or erect rabbit or the dorsal segments of the cow In addition Olson and associates have shown that ligation of a pulmonary artery predisposes to the development of tuberculosis in the segment of lung deprived of its pulmonary artery and in which as a result the alveolar air is similar in composition to room air There may have been some merit in the establishment of sanitoria at high altitudes and there is physiological reason for the clinical impression that pulmonary tuberculosis is particularly apt to develop in children with congenital heart disease and left to right shunts which serve to elevate the oxygen content of the blood in the pulmonary artery

BULLOUS EMPHYSEMA

Communicating vs Noncommunicating Bullae

Bullous emphysema is often indistinguishable from lung cysts Whether it develops from localized partial bronchial obstruction or from primary destruction of lung parenchyma cannot always be determined Some bullae communicate freely with the tracheobronchial tree and are apparently degenerative in origin whereas others are associated with expiratory obstruction within the airway leading to the bulla Such a bulla may be under considerable pressure since air can get in but not out and it may compress adjacent lung tissue and render it functionless

Nitrogen dilution curves may differentiate between communicating and relatively noncommunicating bullae The former produce delayed washout of nitrogen from the lungs during oxygen breathing whereas poorly ventilated bullae produce little abnormality of nitrogen dilution curves since they are almost totally excluded from participation in ventilation and cannot affect the composition of expired air

Abnormal Pulmonary Function

Although bullae may develop in chronic obstructive emphysema bullous emphysema appears to be a different disease, in that generalized airway obstruction is absent A low diffusing capacity has been found in a few adults with this condition This suggests that there is a generalized loss of parenchymal tissue of which the bullae perhaps because of superimposed airway obstruction are but one manifestation Despite the low diffusing capacity, pulmonary hypertension does not appear to be a problem in this disease and patients may live for years without symptoms On the other hand they may develop chronic obstructive emphysema and all of its complications (Chap 6) Spontaneous pneumothorax is often a presenting symptom

Surgery

The indications for surgery in this disease are spontaneous pneumothorax and compression of adjacent lung Opinions vary as to when to excise a bulla for pneumothorax since many patients have a single episode without recurrence Furthermore the bulla may not be demonstrable on x ray However, several episodes of lung collapse are a sufficient indication for surgery This may take the form either of resection of the bulla or of scarification of the pleura as with talcum powder so as to keep the lung from falling away from the chest wall at the time of pneumothorax Talc poudrage is not followed by significant impairment of pulmonary function on the affected side and usually prevents further episodes of lung collapse

Compression of adjacent lung tissue is another indication for surgery Unfortunately, bullous emphysema is often a localized manifestation of generalized disease so that surgical excision of one bulla may be followed by the appearance of another Nevertheless if a bulla is causing obstruction of adjacent lung resection is indicated

LUNG CYSTS

Lung cysts may be single or multiple Solitary cysts are most apt to result from infection particularly tuberculosis Such cysts are generally of no functional consequence but represent a potential source of reactivation of infection Diffuse cystic disease is often of congenital origin but may be difficult to differentiate from severe bronchiectasis Unilateral extensive cystic disease may be associated with extensive expansion of the bronchial collateral circulation (Chap 8)

and with atresia of the ipsilateral pulmonary artery Angiographic distinction between primary and secondary atresia of the pulmonary artery may be difficult

The extent to which cystic disease impairs pulmonary function depends upon the extent to which cysts replace normal lung tissue Surgery can restore little function but may be indicated to control infection Resection of cystic disease does not, per se produce functional impairment

NEOPLASM

Effect on Pulmonary Function

As in cystic disease the functional consequences of pulmonary neoplasm depend upon the amount of lung tissue replaced by tumor Vital capacity and presumably diffusing capacity are reduced in proportion to the amount of tumor tissue present Encroachment on a major bronchus results in airway obstruction and tracheal obstruction with suffocation is a particularly unpleasant form of death Respiratory insufficiency in terms of abnormality of the arterial blood gases is not usually present until late in the course of malignant disease However neoplasms are usually found in older people who may have hypoxemia from coincident pulmonary fibrosis and/or emphysema

Pulmonary Osteoarthropathy

An interesting consequence of bronchogenic carcinoma is clubbing of the fingers and toes pulmonary osteoarthropathy It may occur before the development of other symptoms and in the presence of a relatively small tumor which has produced no detectable abnormality of pulmonary function It may be completely reversed by resection of the tumor and it has disappeared after vagotomy Clubbing is usually not associated with metastatic disease in the lung It may be due to an internal secretion elaborated by the neoplasm It has been reported that the bronchial collateral circulation is greatly expanded in the region of primary but not of secondary lung tumors and it is possible that a similar humoral factor produces growth of the bronchial and digital blood vessels

Surgery

A common problem concerns how much resection of lung tissue can be tolerated by a patient with carcinoma and coexistent pulmo

nary fibrosis and/or emphysema The factors which place a limitation on the amount of lung tissue which can be safely resected and the methods available for evaluating such patients are discussed in Chapter 9 As mentioned there functional considerations must often be disregarded in order to effect complete removal of a tumor, since it is impossible to predict with certainty how much resection can be tolerated by a given patient Occasionally a patient with severe pulmonary insufficiency will tolerate a pneumonectomy despite the poor prognosis implicit in the preoperative measurement of impaired pulmonary function

PLEURAL DISEASE

Pleural disease interferes with pulmonary function primarily by preventing expansion of the underlying lung during inspiration Hypoventilation is usually accompanied by reduction of blood flow, so that the arterial oxygen saturation remains normal The extent of impairment of ventilatory function is readily detected by spirometry Unilateral disease is evaluated by bronchospirometry

Decortication

Decortication of a fibrous peel even if extensive may restore ventilatory function to normal On the other hand longstanding pleurisy particularly if due to tuberculosis may be accompanied by extension of fibrous tissue strands into the lung parenchyma Here the major functional limitation is actually from pulmonary fibrosis, which can be little affected by decortication Since such a lung may receive no ventilation because of the restrictive pleurisy, functional study of the diffusion of gases is impossible Thus, it is impossible to determine whether or not parenchymal fibrosis is present Furthermore, since one cannot predict from function studies the extent to which restorative pleural surgery will be possible it is difficult to determine which patients will benefit from decortication In general, surgery should be done as soon as possible after limiting pleural disease has developed so as to forestall the development of pulmonary fibrosis and an inoperable pleural scar Functional evaluation should be performed periodically in patients with empyema who may be expected eventually to develop a fibrous pleural peel Since one cannot predict which patients with longstanding fibrosis may be benefited by surgery exploratory operation is justified even after several years of known pleural disease

ALVEOLAR VENTILATORY INSUFFICIENCY

Pathophysiology

Chronic alveolar ventilatory insufficiency is a form of functional derangement which usually results from abnormality of the lungs or thoracic cage, or from obesity It occurs when the work of breathing is so great that the patient ventilates his alveoli with subnormal quantities of air rather than do the great amounts of work required to produce a normal alveolar ventilation It may also result from primary depression of the respiratory center In all cases the result is CO_2 retention and hypoxemia

Chest Deformities

Alveolar hypoventilation due to emphysema has been discussed in Chapter 6 Arthritis of the thoracic spine may lead to fixation of the ribs and resultant increase of the work necessary to cause chest expansion Spirometric study reveals diminished vital capacity Kyphoscoliosis causes a similar difficulty and is frequently accompanied by obstructive emphysema with the associated derangements of pulmonary function In contrast to kyphoscoliosis which is frequently accompanied by respiratory impairment pectus excavatum usually produces little cardiopulmonary dysfunction despite the presence of severe deformity Surgery for this disease is advised early in life for cosmetic rather than for functional reasons

Pickwickian Syndrome

The mechanism whereby obesity increases the work of breathing is not entirely clear It seems to be related to the increased work necessary to move the chest and abdomen during respiration This is accentuated in the supine position and hypoxemia and CO_2 retention increase when obese patients lie down The pathophysiologic result of this syndrome is alveolar ventilation insufficient to meet the increased metabolic needs This causes carbon dioxide retention and hypoxemia The elevated arterial P_{co} causes the drowsiness and even narcosis which may be a prominent feature of the disease aptly termed a Pickwickian syndrome from the fat sleepy boy in the Dickens novel Pulmonary hypertension and right ventricular failure may develop when the hypoxemia is severe

Treatment is directed towards improvement of alveolar ventilation and reduction of alveolar ventilatory requirements The former may

be accomplished by ventilatory aids such as positive pressure breathing These are useful in all forms of alveolar hypoventilation Stimulation of the respiratory center by large doses of salicylates or by aminophylline, sometimes in combination with Diamox, may be useful Definitive therapy is removal of the underlying cause of the hypoventilation Weight reduction reduces the work of breathing and thus leads to increased alveolar ventilation It also decreases the metabolic rate, and thus alveolar ventilatory requirements are reduced Weight reduction may cause complete reversal of this syndrome and its sequelae

Although most authors have attributed the clinical features and physiological abnormalities of this syndrome to obesity there is some evidence that primary disease of the brain stem may play a part in the pathogenesis of the sleepiness and hypoventilation For example, hypoventilation is not generally present in obese people and hence factors other than the mechanical effects of obesity may play a part in those patients who do exhibit hypoventilation Obesity may result from a lesion in the hypothalamus and it is conceivable that such a lesion could also cause depression of the respiratory center By the same token the degree of drowsiness seen in this syndrome is often greater than that seen in patients with a greater degree of carbon dioxide retention due to other causes and it is possible that the same central lesion is a factor in producing the hypersomnolence

Primary Depression of the Respiratory Center

As of this writing about five cases of alveolar hypoventilation without discernible cause have been reported Presumably these are the result of lesions in the respiratory center but this conjecture has not been documented by pathological study Diagnosis of this rare abnormality can be made only when alveolar hypoventilation is demonstrated by physiological study and when known causes have been excluded Such a diagnosis is quite likely if alveolar hypoventilation exists in the presence of normal respiratory mechanics

REFERENCES

PULMONARY FIBROSIS

AUSTRIAN R *et al* Clinical and physiological features of some types of pulmonary diseases with impairment of alveolar-capillary diffusion The syndrome of "alveolar-capillary block." *Am J Med 11* 667 1951

Bader M E and Bader R A The alveolar-capillary block syndrome *Am J Med 24* 493 1958

Baldwin E de F Cournand A and Richards D W Jr Pulmonary insufficiency II A study of 39 cases of pulmonary fibrosis *Medicine 28* 1 1949

Cugell D W Marks A Ellicott M F Badger T L and Gaensler E A Carbon monoxide diffusing capacity during steady exercise Comparison of physiologic and histologic findings in patients with pulmonary fibroses and granulomatoses *Am Rev Tuberc & Pulmonary Diseases 74* 317 1956

Harris M S Preuss F S Goldman A and Friedman N Cortisone therapy in Hamman Rich syndrome *Am Rev Tuberc & Pulmonary Diseases 76* 123 1957

Marks A Cugell D W Cadigan J B and Gaensler E A Clinical determination of the diffusing capacity of the lungs Comparison of methods in normal subjects and patients with alveolar-capillary block syndrome *Am J Med 22* 51 1957

West J R *et al* Effects of cortisone and ACTH in cases of chronic pulmonary disease with impairment of alveolar-capillary diffusion *Am J Med 10* 156 1951

Wright G W and Filley G F Pulmonary fibrosis and respiratory function *Am J Med 10* 642 1951

Zohman L R and Williams M H Jr. Cardiopulmonary function in pulmonary fibrosis *Am Rev Resp Dis 80* 700 1959

SARCOIDOSIS

Coates E O and Comroe J H Jr Pulmonary function studies in sarcoidosis *J Clin Invest 30* 848 1951

Marshall R Smellie H Bayliss J H Hoyle C and Bates D V Pulmonary function in sarcoidosis *Thorax 13* 48 1958

Stone D J Schwartz A Feltman J A and Lovelock F J Pulmonary function in sarcoidosis Results with cortisone therapy *Am J Med 15* 468 1953

Williams M H Jr Pulmonary function in Boeck s sarcoid *J Clin Invest 32* 909 1953

TUBERCULOSIS

Anno H and Tomashefski J F Studies on the impairment of respiratory function in pulmonary tuberculosis *Am Rev Tuberc 71* 333 1955

Blair E and Hickam J B Quantitative study of intrapulmonary gas mixing in pulmonary tuberculosis *Am Rev Tuberc & Pulmonary Diseases 74* 343 1956

McClement J H Renzetti A D Jr Carroll D Himmelstein A and Cournand A Cardiopulmonary function in hematogenous pulmonary tuberculosis in patients receiving streptomycin therapy *Am Rev Tuberc 64* 583 1951

Olson B J Scott W H, Jr Hanlon C R and Mattern C F Experimental tuberculosis *Am Rev Tuberc 65* 48 1952

Siebens A A Pietraszek C F Weaver J, and Storey C F Some effects of pneumoperitoneum on respiration in patients with pulmonary tuberculosis *Am Rev Tuberc 70* 672 1954

Soderholm B The hemodynamics of the lesser circulation in pulmonary tuberculosis *Scandinav J Clin & Lab Invest 9* suppl 26 1957

Thomas G I and Jarvis F J Decortication in primary tuberculous pleuritis and empyema with a study of functional recovery *J Thoracic Surg 32* 178 1956

BULLOUS EMPHYSEMA

Baldwin E de F Harken A K Greene D G, Cournand A and Richards D W Jr Pulmonary insufficiency IV A study of 16 cases of large pulmonary air cysts or bullae *Medicine 29* 169 1950

Fitzpatrick M J Kittle C F Lin T K and Dowell J C Some physiologic changes associated with surgical excision of emphysematous bullae *Am J Med 22* 534 1957

Paul J S Beattie E J Jr and Blades B Lung function studies in poudrage treatment of recurrent spontaneous pneumothorax *J Thoracic Surg 22* 52 1951

Knowles J H Gorlin R and Storey, C F Studies of pleural talc poudrage on pulmonary function *J Thoracic Surg 34* 250 1957

Walkup H E, and Wolcott M W Surgical treatment of bullous emphysema *Dis Chest 28* 638 1955

LUNG CYSTS

Cooks F N and Blades B Cystic disease of the lungs *J Thoracic Surg 23* 546 1952

Mannix E, and Haight C Anomalous pulmonary arteries and cystic disease of the lung *Medicine 34* 193 1955

Meador R S and Shields D O Pulmonary cysts Five cases with preoperative and postoperative pulmonary function studies *Am Rev Tuberc & Pulmonary Diseases 75* 53 1957

NEOPLASM AND PLEURAL DISEASE

Semple, T and McCluskie R A Generalized hypertrophic osteoarthropathy in association with bronchial carcinoma *Brit M J 1* 754 1955

Siebens A A Storey C Newman M M Kent D C and Standard J E The physiologic effects of fibrothorax and the functional results of surgical treatment *J Thoracic Surg 32* 53 1956

Wright G W Lee L B Filley G F and Stranahan A Physiologic observations concerning decortication of the lung *J Thoracic Surg 18* 372 1949

ALVEOLAR VENTILATORY INSUFFICIENCY

AUCHINCLOSS J H JR COOK E and RENZETTI A D Clinical and physiological aspects of a case of obesity polycythemia and alveolar hypoventilation *J Clin Invest 34* 1537 1955

BURWELL C S ROBIN E D WHALEY R D and BICKELMAN A G Extreme obesity associated with alveolar hypoventilation—a Pickwickian syndrome *Am J Med 21* 811 1956

CHAPMAN E M DILL D B and GRAYBIEL A The decrease in functional capacity of the lungs and heart resulting from deformities of the chest pulmonocardiac failure *Medicine 18* 167 1939

COATES E O JR BRINKMAN G L and NOE F E Hypoventilation syndrome physiological studies in selected cases *Ann Int Med 48* 50 1958

ESTES E H JR SIEKER H O MCINTOSH H D and KELSER G A Reversible cardiopulmonary syndrome with extreme obesity *Circulation 16* 179 1957

FELTMAN J A NEWMAN W SCHWARTZ, A STONE D J and LOVELOCK F J Cardiac failure secondary to ineffective bellows action of the chest cage *J Clin Invest 31* 762 1952

FISHMAN A P TURINO G M and BERGOFSKY E H The syndrome of alveolar hypoventilation *Am J Med 23* 333 1957

GRAY F D JR Kyphoscoliosis and heart disease *J Chron Dis 4* 499 1956

KERWIN A J Pulmonocardiac failure as a result of spinal deformity *Arch Int Med 69* 560 1942

LAWRENCE I T Idiopathic hypoventilation polycythemia and cor pulmonale *Am Rev Resp Dis 80* 575 1959

LILLINGTON G A ANDERSON M W and BRANDENBURG R O The cardiorespiratory syndrome of obesity *Dis Chest 32* 1 1957

WACHTEL F W RAVITCH M M and GRISHMAN A The relation of pectus excavatum to heart disease *Am Heart J 52* 121 1956

CHAPTER 8

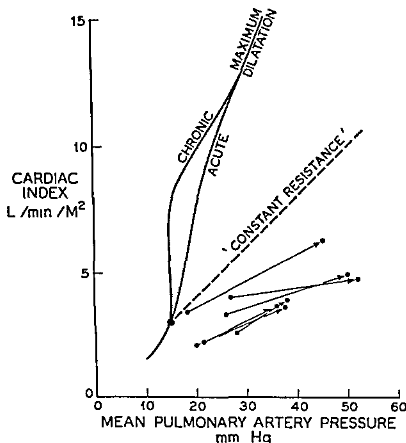
PULMONARY VASCULAR DISEASE

PHYSIOLOGY OF THE PULMONARY CIRCULATION

PRESSURE FLOW VASCULAR RESISTANCE

The normal pulmonary vascular bed is so large in cross section that it offers relatively little resistance to the flow of blood through it The mean pressure in the pulmonary artery is much lower than that in the aorta The pulmonary vascular bed is also capable of expansion either by further dilatation of vessels in use or by opening of other vessels, so that large increases of flow are accompanied by little increase of the pulmonary artery pressure Since the vessels are elastic they increase in diameter when the pressure within them rises Eventually maximal dilatation is achieved and from that point on pulmonary vascular resistance remains little changed as the intraluminal pressure rises This relationship is expressed as the solid acute curve in Figure 20 a plot of blood flow against mean pulmonary artery pressure It is based on available data obtained both from human subjects and experimental animals At subnormal levels of pulmonary artery pressure and flow the vessels are small and the pulmonary vascular resistance is as a result relatively large Elevation of the pressure in the pulmonary artery causes the vessels to dilate so that the pulmonary vascular resistance falls As a result flow increases more than it would if the vascular resistance remained constant At a mean pressure of about 25 mm Hg resistance becomes relatively constant Thereafter increments of pressure result in smaller and relatively constant increments of flow An individual with a normal *pulmonary circulation* can double *his* cardiac output with very little increase of the pressure in his pulmonary artery Further increase of the cardiac output is accompanied by significant rise of pressure

In interpreting the results of studies of the effects of drugs on pulmonary vascular resistance, it must be remembered that the level of the vascular resistance depends upon the intravascular pressure and that agents which alter pulmonary artery pressure will thereby alter pul



Fg 20 R lat onship betwe n card ac index and mean pulmon ry t y pressure the normal lung based on data obta n d in humans and i dogs The sol d ac t l e portrays the ffect of sudden change of flow upo p essure and the chro c l e llust ate the rel t o hip betwee lo g t nd ng ha ge of flow upo p ssu e Th h ded a ea to th h o c l n p e ents th reserve of p lmo ry v lar b d capable of e pa on nder th st etch of o t ued in r a of tral m al pr s The dotted o tant r t e l w dr w from a po t r p s t ng norm l st g p and flow sum g th t th va c lar re tanc r m d consta t as flow nc a d Th s shows how m h th p lmon y a tery pressur wo ld rise as flow incr s d if th r w no co d t xp n on of th p lmonary va lar bed Th point data obt ned o p t nts w th p lmona y mphysema st d d at G land Ho p tal w th d rect m a em t of pulmonary a t ry p ess a d c d c outp t by th F ck princ pl d g rest a d ci Th a ow lead f om th t to th erc point

monary vascular resistance To attribute a vasoconstrictor or vasodilator action to a drug, one must demonstrate a change of vascular resistance at a given level of intravascular pressure not merely a rise or a fall of pulmonary vascular resistance

The curve in Figure 20 represents the effect of acute changes of pressure on flow Chronic studies have shown that sustained increase of flow is followed by a fall of pressure Over a period of time the continuing intraluminal distending force causes further dilatation of the blood vessels in the lung and pulmonary vascular resistance falls A normal individual may have a 5 mm Hg increase of mean pulmonary artery pressure when he first doubles his cardiac output during muscular exercise If he continues to work at the same rate, the pressure will fall in about 4 minutes Similar results have been observed in dogs Acute increase of the blood flow to the perfused lung results in an increase of the pulmonary artery pressure which then falls if the increased rate of perfusion is maintained

This discussion has indicated that the pulmonary vascular resistance is regulated by the intraluminal distending pressure and that mechanical rather than neurogenic factors are responsible for the decrease in pulmonary vascular resistance which accompanies acute or chronic increase of the blood flow to the lung Some individuals believe that vasomotor tone plays a part in the regulation of the size of the pulmonary vascular bed in health and disease Against this concept is the fact that the pressure flow relationships in the experimental perfused denervated lung are similar to those observed in intact humans and dogs The possible role of vasomotor tone in regulating the pulmonary vascular resistance in mitral stenosis has been discussed in Chapter 5 in which it was pointed out that the weight of experimental evidence favors the view that pulmonary vasoconstriction is at best an unimportant factor in causing pulmonary hypertension Likewise, as discussed below reflex vasoconstriction appears to be of little or no importance in the genesis of the pulmonary hypertension that follows pulmonary embolism Vasoconstriction may be important in causing pulmonary hypertension in some forms of congenital heart disease (Chap 3) Thus the number and elasticity of the pulmonary blood vessels and the pressure within them are probably the important factors that regulate the pulmonary vascular resistance in normal subjects Other influences such as vasomotor tone are probably of little consequence if present at all

although they may be important in some types of cardiopulmonary disease

Finally the act of respiration has important effects on the pulmonary circulation Inspiration causes increased blood flow to the lungs because reduction of the intrathoracic pressure causes increased venous return to the thorax In addition pulmonary vascular resistance changes as the dimensions of the lung change The way in which the blood vessels change size depends among other things, upon the degree of lung inflation prior to inspiration and upon the location of the vessels within the lung Some vessels get larger while others get smaller The relationships between lung volume and the dimensions of the various components of the pulmonary vascular bed remain to be defined

EFFECT OF REDUCTION OF PULMONARY VASCULAR BED

Resection of lung tissue results in hemodynamic changes similar to those seen after increase of blood flow to the lung Acute resection of a lobe or a lung causes a small elevation of the pulmonary artery pressure Chronic studies of patients after pneumonectomy have in many instances revealed a normal pulmonary artery pressure in the presence of a normal cardiac output In such cases twice the normal amount of blood is flowing through the remaining lung This effect is denoted by the shaded reserve area in Figure 20 indicating the extent to which in chronic experiments blood flow may increase without change of pulmonary artery pressure Since blood flow may even triple without rise of pulmonary artery pressure the pulmonary vascular bed must be capable of threefold expansion Direct evidence of this is afforded by Wearn s observation that the blood flow through the lung capillaries is intermittent that capillaries open and close but that all the capillaries are not open at the same time

It follows that only marked restriction of the pulmonary vascular bed may be expected to cause significant pulmonary hypertension On the other hand once it develops the blood vessels in the lung are at the limit of their expansibility and an increase of flow or further reduction of the vascular bed will cause substantial increase of the pressure This is similar to the diffusion reserve of the lung which is so large that only extensive impairment causes hypoxemia but once it develops further impairment of diffusion or increase of oxygen

uptake causes great intensification of the arterial oxygen unsaturation (Chap 9)

This concept of a pulmonary vascular bed with a large but not infinite reserve capacity is substantiated by many clinical and experimental findings In patients with pulmonary emphysema, the mean pulmonary artery pressure is only slightly elevated except during periods of severe respiratory insufficiency Muscular exercise causes a sharp increase of the pulmonary artery pressure suggesting a fixed pulmonary vascular resistance The points in Figure 20 represent data obtained on patients having emphysema at Grasslands Hospital Such patients with a greatly increased pulmonary vascular resistance, may have little or no pulmonary hypertension at rest The extent of impairment becomes apparent only during exercise when the pressure in the pulmonary artery rises abnormally Similar data have been obtained on patients with pulmonary vascular restriction secondary to pulmonary fibrosis and to mitral stenosis By the same token experimental pulmonary embolism with glass beads provokes at first, very little increase of a dog s pulmonary artery pressure but once pulmonary hypertension has been produced further injections of embolic material cause large increases of pulmonary artery pressure (see below)

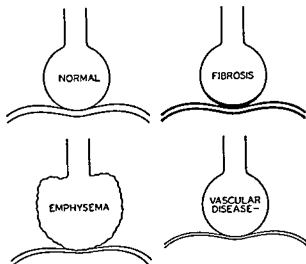
HYPOXIA

This mechanistic concept of the pulmonary vascular bed overlooks what appears to be a valid experimental finding namely that hypoxia causes vasoconstriction in the lung Such a response is teleologically protective by diverting blood flow away from poorly ventilated alveoli and thus preventing hypoxemia This response has been found in experimental animals and in many patients with hypoxemia oxygen breathing has caused reduction of pulmonary hypertension More data with careful measurements of pressure and flow in the pulmonary artery are needed to establish the degree to which hypoxia affects the caliber of the blood vessels in the lung Although hypoxic vasoconstriction may be an experimental reality the degree to which it participates in the genesis of human pulmonary hypertension is uncertain It is likely that the mechanical factors are more important

PULMONARY CIRCULATION IN DISEASE

The pulmonary vascular bed is reduced in pulmonary emphysema Severe pulmonary hypertension in that disease is generally associated

with respiratory insufficiency and appears to be related at least in part to the primary and secondary effects of hypoxemia (Chap 6) In pulmonary fibrosis pulmonary hypertension is a late development and results from anatomical reduction of the pulmonary vascular bed It is often irreversible (Chap 7) The pulmonary hypertension in acquired heart disease usually results from elevation of pulmonary capillary pressure and from the effects of this on the pulmonary vascular bed (Chap 5) The pulmonary hypertension in congenital heart



F'g 21 Types of pulmonary hypertens on In pulmonary fibros s anatom cal red ct on of the p lmo ary vasc l r b d follows al eola th ckeni g so that r duction of the d ffus g capac ty preced s elevat on of the p lmonary art ry pressure In pulmonary mphy ma lo of al ola cap lla ies due to d latat o a d dest uct on of al eol causes the pulmonary hyp rtension wh ch becomes seve o ly wh hypo em a a d polycyth m a d lop P lmo ry hypert ns on due to p mary d a of l g blood s ls may not be accom pa ied by m u able d so der of pulmonary funct on

disease is the result of increased pulmonary blood flow and of primary and secondary changes in the small pulmonary blood vessels (Chap 3)

In this chapter consideration will be limited to primary pulmonary vascular disease and to pulmonary hypertension secondary to pulmonary emboli Figure 21 is a schematic illustration of the genesis of pulmonary hypertension in pulmonary emphysema pulmonary fibrosis and pulmonary vascular disease

PULMONARY EMBOLISM

Pulmonary Hypertenion and Right Heart Failure

For many years, debate has been waged about the importance of reflex vasoconstriction in causing pulmonary hypertension after pulmonary emboli Although vasoconstrictor reflexes are probably present in the lung the pulmonary hypertension that follows pulmonary embolism may be ascribed to mechanical obstruction of blood vessels rather than to reflex vasoconstriction

Injections of aliquots of embolic material into the pulmonary circulation have little effect on the pulmonary artery pressure until large amounts have been injected Once pulmonary hypertension develops it becomes more and more severe on subsequent injections of emboli When severe pulmonary hypertension has been produced in this way in the dog to about 80 mm Hg mean pressure the right heart fails acutely This is manifested by right ventricular dilatation feeble systolic contractions and sudden drop of the pressure in the right ventricle and pulmonary artery while the right atrial pressure rises This reaction is similar to that described by Fineberg and Wiggers after occlusion of the pulmonary artery with a ligature It may be ascribed to the fact that the blood supply to the myocardium limited by decreased flow through the lung is inadequate for the great work load demanded of the heart (Chap 4) Recovery may be spontaneous or may be induced by the injection of adrenalin whereupon the heart begins to beat forcefully again and the systolic pressure in the ventricle rises abruptly coincident with a rise of the pulmonary artery pressure and a fall of the right atrial pressure From this point on the pressure in the pulmonary artery falls gradually, just as it does if the injections of emboli are stopped at any point before the development of right ventricular failure Since there is little passage of embolic material out of the lung and since this same fall of pressure is seen in the isolated perfused lung after embolization, the fall of pressure may be attributed to the opening of blood vessels in the lung under the continuing stimulation of increased intraluminal pressure The rise and fall of pulmonary artery pressure which follows experimental embolization is unaffected by denervation of the perfused lung or by the administration of hexamethonium to the intact animal it does not depend upon nervous reflexes

Sudden death from rather small pulmonary emboli in patients has been cited as evidence that reflex vasoconstriction is important in

causing overwhelming pulmonary hypertension The convincing experiments of Kniseley on wakeful and anesthesized dogs indicate that reflex vasoconstriction is not a factor in causing death after pulmonary embolism in dogs Furthermore evidence that death occurs after a small pulmonary embolus in normal human subjects is lacking Patients with otherwise normal lungs who die from pulmonary emboli have massive involvement, generally of the main pulmonary artery often extending back into the right ventricle On the other hand patients with a limited pulmonary vascular reserve may develop overwhelming pulmonary hypertension after a rather small embolus

Hypoxemia

Recovery from right heart failure after experimental pulmonary embolism is generally associated with the sudden appearance of hypoxemia This is completely overcome by the inspiration of as little as 40 per cent oxygen and may be attributed to reduction of the diffusing capacity of the lung This is due to the fact that all the blood is flowing through a few dilated capillaries and the surface and contact time available for diffusion is greatly reduced As more blood vessels open in the lung as manifested by a reduction of the pulmonary artery pressure the oxygen saturation rises to normal There is a close parallel between the diffusion and circulation reserves of the lung and severe reduction of the pulmonary vascular bed to the point of overwhelming pulmonary hypertension is accompanied by hypoxemia due to coincident limitation of the diffusing capacity

Tachypnea

Although reflex vasoconstriction appears to be of little consequence in the pathogenesis of pulmonary hypertension due to pulmonary embolism reflexly induced tachypnea has been amply demonstrated This accounts for the increase of respiratory rate and the dyspnea associated with pulmonary emboli Such hyperventilation causes reduction of the arterial P_{co} but fails to improve the hypoxemia the latter being due to impaired diffusion of oxygen rather than to reduced alveolar oxygen tension

Treatment

A number of therapeutic implications emerge from this discussion In the first place atropine or autonomic blocking agents may be

expected to exert no effect on the increased pulmonary vascular resistance after pulmonary emboli This is the case in the experimental animal and clear cut clinical evidence of the value of this type of medication is lacking Indeed such drugs may be contraindicated because of adverse effects on the circulation

In the second place the shock which may follow pulmonary emboli should be treated with pressor agents Epinephrine has proved to be lifesaving in dogs Digitalis is indicated to improve right ventricular performance but may have little effect

Third if the patient can be tided over the acute episode of pulmonary embolism recovery may be anticipated and may be more or less complete as new blood vessels open in the lung Dogs have been subjected at monthly intervals to three episodes of pulmonary embolism each sufficient to provoke acute right ventricular failure, on each occasion the pulmonary artery pressure was normal at the start of the *second and third embolizations Indeed just as much* embolic material was required to provoke severe pulmonary hypertension at the third embolization as had been used initially

Fourth oxygen breathing is of therapeutic value in patients who have experienced severe pulmonary embolism whether or not cyanosis an imperfect sign of hypoxemia is present Since an adequate effect on the arterial oxygen saturation may be achieved with the inspiration of 40 per cent oxygen in the experimental animal an oxygen tent is a satisfactory and comfortable form of oxygen administration in this situation

Finally since the hypoxemia may be controlled by oxygen, and since the arterial P_{co} is reduced morphine should be used for the treatment of dyspnea The latter is largely the result of reflex tachypnea and disappears if ventilation is reduced

PULMONARY HYPERTENSION DUE TO CHRONIC PULMONARY VASCULAR DISEASE

Pathogenesis and Treatment

Chronic elevation of the pressure in the pulmonary artery develops in patients who suffer repeated attacks of pulmonary embolism It is due to pathologic changes in the pulmonary arteries which are *indistinguishable* from primary pulmonary arteriosclerosis In both primary and secondary pulmonary vascular disease pulmonary hypertension is greatly aggravated by increased blood flow as during

exercise This may cause substernal pain not unlike that of angina though it is generally higher in location rarely described as con stricting and rarely responds to the administration of nitroglycerine Convincing evidence has not been advanced that the pulmonary hypertension in either primary or secondary vascular disease is the result of reflex vasoconstriction Attempts at lowering the pulmonary artery pressure with ganglionic blocking agents have not proved very satisfactory Since further reduction of a limited pulmonary vascular bed may be disastrous long term treatment with anticoagulants would appear to be a logical approach in order to prevent occlusion of more pulmonary vessels Adequate clinical assessment of therapy of this type is not at hand

Patients with chronic pulmonary hypertension due to pulmonary vascular disease are unusually brittle and subject to sudden death Since they may be at the point at which slight reduction of the pulmo nary vascular bed or minor increase of the blood flow and oxygen consumption may lead to overwhelming pulmonary hypertension and hypoxemia they must be carefully sheltered They should not fly over 5000 feet and should not exercise and they represent real risks for study by cardiac catheterization angiocardiography or ganglionic blocking agents Sudden death has occurred after all three of these procedures Although little can be done to reverse the pulmonary vascular changes that have taken place progression might be avoided by the use of anticoagulant therapy the single promising therapeutic weapon available at this time

Hypoxemia

Hypoxemia may be present in this form of chronic pulmonary hypertension and is generally due to reduction of the diffusing capac ity It is readily overcome by oxygen breathing Less commonly hypoxemia may be due to a right to left shunt The foramen ovale which is probe patent in about 25 per cent of autopsies may open when the pressure in the right atrium rises after right ventricular failure The sudden appearance of hypoxemia which is not relieved by breathing oxygen suggests the development of this complication Surgical closure of such a defect is contraindicated since it prevents overloading of the right ventricle and closure might result in more severe right ventricular failure (Chap 3)

PULMONARY ARTERIOVENOUS FISTULA

Experimentally, large glass spheres may pass directly through arteriovenous communications in the dog lung but evidence of functioning pulmonary arteriovenous fistulas in human subjects is lacking Such communications might be responsible for hypoxemia in some patients with pulmonary hypertension if the channels opened under the stress of increased pulmonary artery pressure Direct experimental verification of this possibility is lacking

Pulmonary arteriovenous fistula, a hereditary disorder often associated with systemic telangiectasia may cause hemoptysis or if the fistula is large hypoxemia Surgical excision is indicated for this lesion but multiple fistulas may be present, and resection of one may be followed by the appearance of others Nevertheless significant hypoxemia or hemoptysis are sufficient indications for surgery Chest x ray usually suffices to depict these lesions and angiography will define the doubtful case The magnitude of the right to left shunt is reflected in the degree of hypoxemia present, a useful functional test (Chap 11)

Multiple pulmonary arteriovenous fistulas may develop in cirrhosis of the liver Cases of cirrhosis have been described with this abnormality, and the finding of reduced arterial oxygen saturation in many other patients with cirrhosis suggests the presence of such right to left shunts It is possible that pulmonary arteriovenous fistulas develop from the same humoral stimuli that produce cutaneous spider nevi

BRONCHIAL COLLATERAL CIRCULATION

The bronchial circulation a part of the systemic vascular bed is small in normal human subjects and dogs Ligation of a pulmonary artery or suppurative disease of the lung, particularly bronchiectasis is followed by marked expansion of this vascular bed one factor in the occasionally severe hemoptysis that occurs in bronchiectasis Since these vessels are systemic arteries the pressure in them is high and a ruptured bronchial artery tends to bleed profusely and to cause hemoptysis of arterial rather than of venous blood

AFTER LIGATION OF A PULMONARY ARTERY

After ligation of a pulmonary artery the expanded bronchial collateral bed is of functional significance in that it supplies blood to the

lung formerly supplied by that pulmonary artery Since the collateral flow is made up of arterial blood already fully saturated with oxygen there is no appreciable oxygen uptake by such a lung The lung de prived of its pulmonary artery ventilates normally but consumes no oxygen

IN SUPPURATIVE DISEASE

These vessels may serve another function in disease Elevation of the pressure in the capillaries into which the bronchial collaterals drain serves to prevent the flow of unsaturated blood from the pulmo nary artery through diseased areas of lung This prevents the hypox emia which would otherwise result from a functional right to left shunt It may explain the fact that the arterial oxygen saturation is often normal in extensive bronchiectasis the poorly ventilated bron chiectatic areas presumably being deprived of pulmonary artery blood flow by the expanded bronchial collateral bed

A dramatic case of bronchiectasis with marked overexpansion of the bronchial circulation has recently been reported by Alley and his associates In this patient the bronchial collaterals were so large in the left lung the seat of extensive bronchiectasis that dye injected into the main pulmonary artery failed to enter the left pulmonary artery at all Dye injected into the aorta clearly filled the left pulmo nary artery by retrograde perfusion from the bronchial arteries In this patient hypoxemia was prevented but the increased collateral flow represented a burden to the left ventricle which had to pump the normal cardiac output plus the tremendous circulation that went round and round through the bronchial arteries It may be difficult to distinguish such a situation from agenesis of the pulmonary artery since in each case conventional angiography may fail to demonstrate the pulmonary artery on the involved side It is possible that some cases diagnosed as congenital atresia of the pulmonary artery with secondary bronchiectasis actually represent bronchiectasis with a greatly expanded bronchial collateral bed which caused reversal of the blood flow through that pulmonary artery

REFERENCES

PHYSIOLOGY OF THE PULMONARY CIRCULATION

COURNAND A Pulmonary circulation *Science 125* 1231 1957
DEXTER L *et al* Studies of the pulmonary circulation in man at rest Normal

variations and the interrelations between increased pulmonary blood flow elevated pulmonary arterial pressure and high pulmonary capillary pressures *J Clin Invest 29* 602 1950

FINEBERG M H and WIGGERS C J Compensation and failure of the right ventricle *Am Heart J 11* 255 1936

FISHMAN A P McCLEMENT J HIMMELSTEIN A and COURNAND A Effects of acute anoxia on the circulation and respiration in patients with chronic pulmonary disease studied during the steady state *J Clin Invest 31* 770 1952

FRITTS H W JR HARRIS P CLAUSS R H ODELL J E and COURNAND A The effect of acteylcholine on the human pulmonary circulation under normal and hypoxic conditions *J Clin Invest 37* 99 1958

HAMILTON W F The physiology of pulmonary circulation *J Allergy 22* 3 397 1951

HEIMAN D F RODBARD S SHAFFER A B and SNIDER G L Respiratory factors affecting pulmonary arterial blood pressure and flow through the lungs *J Appl Physiol 10* 31 1957

ROOS A THOMAS L J JR NAGEL E L and PROMMAS D C Pulmonary vascular resistance as function of right ventricular left auricular intra pulmonary and pleural pressures *Fed Proc 16* 109 1957

WEARN J T ERNSTENE A W BROMER A W BARR J S GERMAN W J and ZSCHIESCHE L J Normal behavior of pulmonary blood vessels with observations on the intermittence of the flow of blood in the arterioles and capillaries *Am J Physiol 109* 236 1934

WILLIAMS M H JR Relationships between pulmonary artery pressure and blood flow in the dog lung *Am J Physiol 179* 243 1954

PULMONARY CIRCULATION IN DISEASE

BORDEN C W EBERT R V WILSON R. H and WELLS H S Pulmonary hypertension in heart disease *New England J Med 242* 529 1950

BRILL I C Cor pulmonale a semantic consideration with brief notes on diagnosis and treatment *Mod Concepts Cardiovas Dis 26* 425 1957

CARROLL D Chronic obstruction of major pulmonary arteries *Am J Med 9* 175 1950

CASTELFRANCO M and CORNIA G Physiological pathology and pathogenesis of chronic cor pulmonale in the light of experimental findings in man and animals *Folia Cardiol 14* 215 1955

CHAPMAN D W ABBOTT J P and LATSON J Primary pulmonary hyper tension Review of literature and results of cardiac catheterization in ten patients *Circulation 15* 35 1957

COURNAND A Some aspects of the pulmonary circulation in normal man and in chronic cardiopulmonary diseases *Circulation 2* 641 1950

CUTLER J G NADAS A S GOODALE W T HICKLER R B and RUDOLPH A. M Pulmonary arterial hypertension with markedly increased pulmonary resistance *Am J Med 17* 485 1954

DOYLE A E GOODWIN J F HARRISON C V and STEINER R E Pulmonary vascular patterns in pulmonary hypertension *Brit Heart J* *19* 353 1957

FISHMAN A P and RICHARDS D W Jr The management of cor pulmonale in chronic pulmonary disease with particular reference to the associated disturbances in the pulmonary circulation *Am Heart J* *52* 149 1956

KNISELY W H WALLACE J M MAHALEY M S JR and SATTERWHITE M M Evidence including in vivo observations suggesting mechanical blockage rather than reflex vasospasm as the cause of death in pulmonary embolism *Am Heart J* *54* 483 1957

KUIDA H DAMMIN G J HAYNES F W RAPAPORT E and DEXTER L Primary pulmonary hypertension *Am J Med* *23* 166 1957

O NEAL R M and THOMAS W A The role of pulmonary hypertension and thromboembolism in the production of pulmonary arteriosclerosis *Circulation* *12* 370 1955

PARKER B M and SMITH J R Pulmonary embolism and infarction A review of the physiologic consequences of pulmonary arterial obstruction *Am J Med* *24* 402 1958

SHEPHERD J T EDWARDS J E BURCHELL H B SWAN H J C and WOOD E H Clinical physiological and pathological considerations in patients with idiopathic pulmonary hypertension *Brit Heart J* *19* 70 1957

TOSETTI R L Resistance zones in the pulmonary circulation in the course of mitral stenosis and in chronic cor pulmonale due to emphysema *Arch mal cœur* *48* 346 1955

WHITTERIDGE D Multiple embolism of the lung and rapid shallow breathing *Physiol Rev* *30* 475 1950

WILLIAMS M H JR Mechanical vs reflex effects of diffuse pulmonary embolism in anesthetized dogs *Circulation Res* *4* 325 1956

YU P N *et al* Pulmonary capillary pressure in various cardiopulmonary diseases at rest and under stress *Am Heart J* *49* 31 1955

PULMONARY ARTERIOVENOUS FISTULA

GRAY F D JR LURIE P R and WHITTEMORE R Circulatory changes in pulmonary arterio venous fistula *Yale J Biol & Med* *25* 107 1952

RYDELL R and HOFFBAUER F W Multiple pulmonary arteriovenous fistulas in juvenile cirrhosis *Am J Med* *21* 450 1956

TOBIN C E and ZARIQUIEY M O A V shunts in the human lung *Proc Soc Exper Biol & Med* *75* 827 1950

BRONCHIAL COLLATERAL CIRCULATION

ALLEY R D STRANAHAN A KAUSEL H FORMEL P and VAN MIEROP L H S Demonstration of bronchial pulmonary artery reverse flow in suppurative pulmonary disease *Clin Res* *6* 41 1958

GRAY F D JR. LURIE P R and WHITTEMORE R Circulatory changes in

chronic pulmonary diseases a study of pulmonary collateral circulation. *Yale J Biol & Med* *23* 380 1951

LIEBOW, A A HALES M R HARRISON W BLOOMER W and LINDSKOG G E The genesis and functional implications of collateral circulation of lungs *Yale J Biol & Med* *22* 637 1950

ROOSENBURG J G and DEENSTRA H Bronchial pulmonary vascular shunts in chronic pulmonary affections *Dis Chest* *26* 644 1954

SHEDD D P, ALLEY, R. D and LINDSKOG C E Observations on the hemodynamics of bronchial pulmonary vascular communications *J Thoracic Surg* *22* 537 1951

CHAPTER 9

PHYSIOLOGICAL CONSIDERATIONS IN THORACIC SURGERY

Evaluation of pulmonary function is frequently sought for the patient with pulmonary disease who is being considered for thoracic surgery Although data have been obtained on the effects of various surgical procedures on ventilatory function and some information is at hand about the degree to which impaired ventilatory function reduces an individual s chances of surviving various surgical procedures it is impossible to use such data to make absolute decisions for individual patients nor should one expect to be able to do this There is little reason why an individual s level of ventilatory function should have bearing on his chances of developing chest wall or other postoperative complications such as bronchopleural fistula or pleural effusion These complications are major factors in morbidity and mortality following thoracic surgery Furthermore ventilatory function is only one and possibly not the most important aspect of pulmonary function Finally the functional loss following resection is in large part related to the amount of function present preoperatively in the resected lung Since thoracic surgery generally involves removal of diseased or nonfunctioning lung tissue it may even lead to improvement of pulmonary function

RESECTION OF LUNG TISSUE

CIRCULATION AND DIFFUSION

What are the important aspects of a patient s pulmonary functional status that should be considered in deciding for or against thoracic surgery? A major consideration is not to remove so much lung tissue that pulmonary insufficiency in terms either of arterial blood gas

abnormality or of undue restriction of the pulmonary vascular bed, will ensue In analyzing the ways in which resection might encroach on pulmonary functional reserve, one can draw on information ob tained from animal experiments It has been found that resection of up to 75 per cent of a dog s lung is without significant effect Ventila tory function is adequate since sufficient alveolar ventilation may be provided with intermittent inspiratory positive pressure to maintain the arterial carbon dioxide tension at 40 mm Hg Analysis of the alveolar and arterial blood gas tensions has revealed that there is no increase of the alveolar arterial oxygen tension difference indicating that the distribution of blood and gas flows throughout the lung was not impaired Pulmonary hypertension was mild or absent

Further resection of pulmonary tissue results in the rather sudden appearance of profound hypoxemia and/or right heart failure The hypoxemia has been found to result from reduction of the diffusing capacity of the lung and it can be completely overcome by having the dog breathe as little as 40 per cent oxygen Apparently resection of large amounts of pulmonary tissue causes such a reduction of alveolar capillary surface area that oxygen cannot diffuse into the alveolar capillary blood fast enough to raise the arterial oxygen saturation to normal levels It is of interest that this point of critical reduction of the diffusing capacity coincides with the development of severe pul monary hypertension and in many instances of right heart failure This indicates that the limits of pulmonary capillary reserve im portant for diffusion and of pulmonary arteriolar reserve concerned in pulmonary vascular resistance are similar

These experiments indicating that in the normal lung the diffusion and circulatory functions limit a dog s ability to tolerate removal of pulmonary tissue may have little bearing on the evaluation of the patient with pulmonary disease for chest surgery However they pro vide a starting point and suggest that attention should be paid to these functions in assessing patients with impaired pulmonary function Thus it may be possible to predict on the basis of the maximal dif fusing capacity of the lung how much functioning tissue may be resected with safety Another step in this direction is the measurement of the pressure in the pulmonary artery before and after the branch of the pulmonary artery to the portion of the lung to be resected is occluded by a balloon located on the distal end of a double lumen cardiac catheter If after occlusion of the vessel the pressure in the

main pulmonary artery rises sharply the patient is deemed a poor risk for surgery Another and somewhat simpler approach is to measure the pulmonary artery pressure during muscular exercise sufficient to increase the total pulmonary blood flow to a level equivalent to that which will be flowing through the remaining lung after resection For example if one is planning a pneumonectomy one may measure the pulmonary artery pressure during exercise which causes doubling of the resting cardiac output During this exercise, the entire lung is subjected to an increase of flow similar to that to which the nonresected lung will be subjected postoperatively at rest If pulmonary hypertension is severe surgery may be hazardous The degree to which such studies of circulation and diffusion in the lung may be of practical prognostic value in thoracic surgery remains to be proved The added stresses of anesthesia thoracotomy pulmonary collapse and postoperative reduction of ventilation and cough are variable and hard to predict Certainly the psychic factors leading to courageous attempts at good postoperative assistance by the patient are of importance and yet cannot be measured objectively

The foregoing methods of analysis are mainly concerned with the question of how much normally functioning tissue may be safely removed This is not always a problem since in many diseases resection is largely restricted to removal of diseased lung However this problem is present in cancer surgery in which large amounts of normal lung may be resected along with the tumor It must be borne in mind that the objective of cancer surgery is to remove all of the tumor this may override all functional considerations If the surgeon finds that he must carry out a pneumonectomy in order to accomplish his mission the functional status of the patient should not necessarily deter him On the other hand when the surgeon has the opportunity of doing a lesser degree of resectional surgery without really knowing that the more radical procedure is necessary functional considerations become extremely important

VENTILATORY TESTS

Preoperative evaluation by study of pulmonary circulation and diffusion is so technically difficult and of such recent origin that its practical value remains to be determined Of what value is the more conventional evaluation of pulmonary function that is measurement of ventilatory function and perhaps of arterial blood gases? In gen

eral, if severe obstructive disease is present as evidenced by a maximal breathing capacity below 40 liters per minute or an M M F less than 50 liter per second or if severe restrictive disease is present with a vital capacity less than 25 per cent of the predicted value the patient is a poor risk for surgery He is apt either not to survive the procedure or to have pulmonary insufficiency if he does survive The risk increases if the arterial oxygen saturation is below 90 per cent unless the hypoxemia is due to circulation of blood through diseased lung which will be removed at surgery Finally carbon dioxide retention indicates further impairment of pulmonary function and corresponding increase of the surgical risk

These very general yardsticks of pulmonary functional status are useful adjuncts to the over all clinical evaluation of the patient for thoracic surgery but they may eventually be replaced by more specific tests of various discrete aspects of pulmonary function Different tests may be necessary in different diseases The diffusing capacity may be the important measurement in patients with pulmonary fibrosis, the airway resistance in patients with emphysema and the pulmonary vascular resistance in patients with pulmonary vascular disease In doubtful cases as many measurements as possible should be obtained

Bronchospirometry

Bronchospirometry is a special form of study designed to obtain information about the functional status of each lung separately The technique involves passage of a double lumen catheter into the left main bronchus Air goes in and out of the left lung through an opening at the tip of the catheter which is sealed by a balloon just proximal to the tip The other lumen opens into the trachea and when the distal and another proximal balloon are inflated serves as a passageway for all of the air entering and leaving the right lung It is then possible to record the ventilation of each lung separately and by connecting each lung to an oxygen filled spirometer containing soda lime to measure the oxygen consumption of each lung (Fig 22)

Bronchospirometry provides separate measurement of the ventilatory function and of the oxygen consumption of each lung The latter is of paramount importance representing the net functional capacity of each lung A lung deprived of its pulmonary artery may ventilate normally but does not take up oxygen and is useless to the patient On

the other hand, a lung encased in fibrotic pleura may have very little ventilation Yet if alveolar capillary function is normal it may extract large amounts of oxygen from the alveolar air and be of great

	Per Cent Oxygen Cons	Total Vital Cap
Right	85	89
Left	15	11

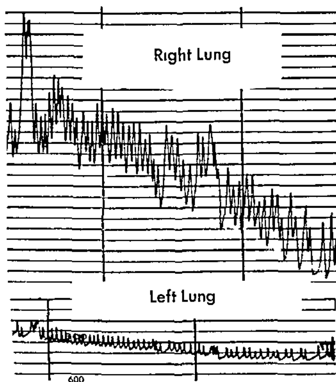


Fig 22 Bo chosp rom t c co d from a pat nt w th a left fibrothorax Th mo k d r duct on of oxygen co mpt o and of vent l t on nd te that fu ct on p act cally ab t o th left s de a posit i d cat on for deca t t on and al o a nd cation that a left pn mo ectomy co ld b performed w tho t f ther sig n ficant decrea of pulmonary fu ct o

functional consequence to the patient Bronchospirometric study by delineating the degree to which each lung participates in oxygen uptake is a guide to the functional importance of a lung being considered for surgery This does not apply only to patients being considered for pneumonectomy An individual with generalized pulmonary disease being evaluated for lobectomy must be considered in the light of possible postoperative complications such as atelectasis or bronchopleural fistula which might act at least temporarily like a pneumonectomy If an individual with borderline pulmonary reserve is relying heavily on one lung for his oxygen consumption that lung probably should not be approached surgically at all On the other hand a functionless lung may be resected without causing further loss of pulmonary function

OVERDISTENTION OF REMAINING LUNG

A problem which is far from settled concerns the development of overdistention of the remaining lung after resection and whether or not thoracoplasty is indicated in order to prevent such a development Certainly herniation of lung into the contralateral thorax with obstruction of the airways is undesirable but that distention of ipsilateral or contralateral lung is harmful cannot be said with certainty It would appear from the limited observations available to date that such distention is not equivalent to chronic pulmonary emphysema since it is not associated with evidence of airway obstruction In this sense it is not harmful On the other hand since increase of lung volume does not necessarily improve pulmonary function there would appear to be little to gain from such overdistention A reasonable approach is to strive to achieve a normal state of inflation of the lung being left in the chest and at the same time to preserve maximal bellows action of the chest wall Thus it might not be harmful to let one lobe fill one side of the chest On the other hand if this could be prevented by a small thoracoplasty which did not interfere with chest expansion thoracoplasty might be desirable By the same token in the absence of fixation of the mediastinum thoracoplasty would appear to be desirable after pneumonectomy An exception to this general plan is surgery on infants and small children in whom there appears to be a real capacity for regeneration of pulmonary tissue Under these circumstances it is advisable to leave space for the lung to grow into We have studied one boy in his late teens who had had

a pneumonectomy in childhood At the time of study, he had absolutely normal ventilatory function and only slight reduction of his diffusing capacity Thoracoplasty would probably have deprived him of the chance to develop this much functioning pulmonary tissue

THORACOPLASTY

Although resection of diseased lung is the most common form of surgical therapy of tuberculosis today thoracoplasty is still used in selected cases Since the procedure is not attended by many of the complications that may follow resection such as bronchopleural fistula or tuberculous empyema it may be employed in patients whose functional status might not allow them to survive such developments In general collapse of a segment of lung seems to result in about the same functional loss as occurs after resection of the segment but patients with pulmonary insufficiency may tolerate thoracoplasty when they could not go through an equivalent resection

The physiological approach to thoracic surgery has had a good deal of effect on the type and extent of thoracoplasty that surgeons perform For example much of the functional loss that followed thoracoplasty many years ago was found to result from scoliosis It was also found that if the transverse processes of the vertebrae were preserved good collapse could be achieved without the development of scoliosis The effects of various thoracoplasties and other collapse procedures have received extensive evaluation by bronchospirometric and ventilatory function study

PHYSIOLOGICAL INDICATIONS FOR THORACIC SURGERY

Another aspect of physiological evaluation prior to thoracic surgery concerns positive indications for surgery Does a given lesion constitute a sufficient physiological problem to warrant resection? Bullous emphysema is one example of this Chest x ray may reveal one or more bullae but that they are impairing ventilatory function by pressure on adjacent lung may best be determined by ventilatory studies The symptoms produced by such bullae may be determining factors in the decision for surgery but function studies may also provide a positive indication for surgical intervention

Similarly the extent to which a fibrous peel interferes with ventila

tory function may be determined by bronchospirometry and if functional impairment exists this may be the important factor in deciding to perform surgery (Fig 22) The degree to which blood flows through a pulmonary arteriovenous fistula and, hence the severity of that lesion, is reflected in the degree of hypoxemia present There are other examples, but these illustrate how analysis of the extent to which a disease or abnormality interferes with pulmonary function is important in selecting patients for thoracic surgery

REFERENCES

ADAMS W E PERKINS J F JR FLORES A CHAO P and CASTELLANOS M The significance of pulmonary hypertension as a cause of death following pulmonary resection *J Thoracic Surg 26* 407 1953

BIRATH G and SODERHOLM B Bronchospirometric investigations before and after a small thoracoplasty *Am Rev Tuberc & Pulm Dis 75* 724 1957

BIRATH G SWENSON E W ANDER L and BERGH N P The definitive functional results after partial pulmonary resection Bronchospirometric investigation *Am Rev Tuberc & Pulmonary Diseases 76* 983 1957

BLAIR E and HICKAM J B Intrapulmonary gas mixing following lung surgery With particular reference to tuberculosis *Am Rev Tuberc & Pulmonary Diseases 78* 1 1958

BROFMAN B L CHARMS B L KOHN P M ELDER J NEWMAN R and RIZIKA M Unilateral pulmonary artery occlusion in man *J Thoracic Surg 34* 206 1957

COURNAND A RILEY R L HIMMELSTEIN A and AUSTRIAN R Pulmonary circulation and alveolar ventilation perfusion relationships after pneumonectomy *J Thoracic Surg 19* 80 1950

DRESSLER S H BRONFIN G J and GROW J B Pulmonary function studies before and after extrapleural pneumonolysis with plombage *J Thoracic Surg 19* 938 1950

ETSTEN B E OVERHOLT R H WALKER J H and REYNOLDS R N Pulmonary function after segmental pulmonary resection for bronchiectasis *New England J Med 248* 81 1953

GAENSLER E A and STRIEDER J W Progressive changes in pulmonary function after pneumonectomy the influence of thoracoplasty pneumothorax oleothorax and plastic sponge plombage on the side of pneumonectomy *J Thoracic Surg 22* 1 1951

GORLIN R KNOWLES J H and STOREY C F Effects of thoracotomy on pulmonary function *J Thoracic Surg 34* 242 1957

HANSON H E Temporary unilateral occlusion of the pulmonary artery in man A method for preoperative determination of the function of each lung *Acta chir scandinav* Suppl 187 1954

LINDAHL, T Spirometric and bronchospirometric studies in five rib thoracoplasties *Thorax* 9 285 1954

MARTIN F E and STEAD W W Physiologic studies following thoracic surgery III Ventilatory studies in the immediate postoperative period. *J Thoracic Surg* 25 417 1953

POWERS S JR. and HIMMELSTEIN A. Late changes in ventilatory function following thoracoplasty *J Thoracic Surg* 22 45 1951

SCHILLING J A HARVEY R. B BALKE B and RATTUNDE, H F Extensive pulmonary resection in dogs altitude tolerance work capacity and pathologic physiologic changes *Ann Surg* 144 635 1956

SLOAN H MORRIS J D FIGLEY M and LEE R. Temporary unilateral occlusion of the pulmonary artery in the preoperative evaluation of thoracic patients *J Thoracic Surg* 30 591 1955

STEAD W W Physiologic studies following thoracic surgery II Immediate effects of upper lobectomy combined with a five rib thoracoplasty *J Thoracic Surg* 25 194 1953

STEAD W W and SOUCHERAY P H Physiologic studies following thoracic surgery I Immediate effects of thoracoplasty *J Thoracic Surg* 23 452 1952

TAYLOR, F H ROOS A. and BURFORD T H *Respiratory and circulatory* studies in patients after bilateral lobectomy *J Thoracic Surg* 20 974 1950

VARGHA, G Lung resections in the light of function studies *Ztschr Tuberk* 106 154 1955

WILLIAMS M H JR CANNEY P C and RAYFORD C R. The acute effects of resection of pulmonary tissue on some pulmonary functions in the dog *J Thoracic Surg* 31 623 1956

WOODRUFF W MERKEL C. G and WRIGHT G W Decisions in thoracic surgery as influenced by the knowledge of pulmonary physiology *J Thoracic Surg* 26 156 1953

CHAPTER 10

ACUTE DISORDERS OF PULMONARY FUNCTION

Experimental studies, both in man and in animals, have *revealed the nature of the physiological disturbances that accompany* many acute disorders of pulmonary function and have provided the basis for rational therapy of such problems In this chapter, the *pathophysiology of pulmonary edema, of atelectasis, and of pneumothorax* will be discussed and the physiological basis for application of artificial respiration will be outlined Another acute disorder of *pulmonary function, pulmonary embolism has been discussed in* Chapter 8

PULMONARY EDEMA

PATHOGENESIS

The formation of edema fluid is based on Starling's law of fluid transfer across capillary walls This law states that filtration out of a capillary is directly proportional to the intracapillary pressure minus the extracapillary (tissue) pressure and is inversely proportional to the effective osmotic pressure of the blood In normal individuals, there is a continuous transudation of fluid across the alveolar capillary walls This fluid is returned to the venous system by the lymphatics When excessive transudation occurs, fluid remains in the alveoli and small airways as pulmonary edema Interference with lymphatic drainage a little-explored field should contribute to the development of pulmonary edema Other factors which lead to pulmonary edema are decrease of the osmotic pressure of the blood increased pulmonary capillary pressure and increased permeability of the lung capillaries

Decreased osmotic pressure is rarely, if ever, the sole cause of

pulmonary edema but hypoalbuminemia may be a contributing factor Increased capillary pressure results from venous congestion This may be the result of (1) a high left ventricular end-diastolic pressure in the failing or loaded" heart (Chap 4), (2) elevated left atrial pressure in mitral stenosis or atrial myxoma (Chap 5) or (3) occlusion of pulmonary veins The hypervolemia accompanying heart failure accentuates the pulmonary capillary hypertension Pulmonary edema due to increased capillary permeability is seen after administration of certain poisons and after inhalation of steam

The pulmonary edema accompanying acute disease of the central nervous system has long been a perplexing problem Sarnoff and associates have produced pulmonary edema in experimental animals by injecting fibrin into the region of the medulla oblongata This led to systemic vasoconstriction with resultant elevation of the pulmonary capillary pressure due to pooling of blood in the lungs A therapeutic corollary to this work is the fact that ganglionic blocking agents which cause systemic vasodilatation and, hence a shift of blood from the pulmonary to the systemic venous bed are effective therapeutic agents in some patients with pulmonary edema particularly those with hypertension

TREATMENT

The treatment of pulmonary edema should be directed at removal of the specific underlying cause In addition certain general effects of pulmonary edema require therapy This therapy is based on knowledge of how pulmonary edema alters pulmonary function

In essence pulmonary edema consists of abnormal quantities of fluid in the alveoli airways and interstices of the lung One of the first demonstrable abnormalities of pulmonary function is reduction of the lung compliance There is also reduction of the vital capacity a cruder but more readily available means of assessing the amount of pulmonary edema present In addition hyperpnea a reflex effect of pulmonary congestion develops early This coupled with the increased work of breathing due to the reduced lung compliance accounts for the development of dyspnea The tachypnea is associated with reduced arterial carbon dioxide tension and since it effects little improvement of the hypoxemia which may be present (see below) it should be treated by the administration of morphine The clinical value of morphine in pulmonary edema may be ascribed to this reduc

tion of tachypnea and, hence, of dyspnea and to its central depressant actions with alleviation of anxiety

Hypoxemia appears later It may be relatively slight in what appears to be severe pulmonary edema and its degree correlates poorly with the clinical severity Studies on dogs have revealed that it is due to an effective right to left shunt so that the arterial oxygen saturation is only slightly elevated by the inspiration of oxygen This shunt is probably the result of occlusion of small airways by edema fluid and foam so that large numbers of alveoli are totally un ventilated the blood flowing through them is not exposed to alveolar air Diffusion in the alveoli that are normally ventilated appears to be adequate An immediate consequence of this is the fact that oxygen breathing has little effect on the hypoxemia and cyanosis present in pulmonary edema On the other hand anti foaming agents and the administration of oxygen with inspiratory positive pressure which tends to force air through the congested airways, may over come the hypoxemia The latter therapy has the additional advantage of raising the intra alveolar pressure so that (1) the rate of forma tion of edema fluid is decreased and (2) blood is shifted out of the pulmonary vascular system into the systemic veins This in turn lowers pulmonary capillary pressure and reduces the tendency to wards formation of edema The application of tourniquets has a similar effect on the distribution of blood, and keeping the abdomen legs and arms at a lower level than the chest is also of value

ATELECTASIS

PATHOGENESIS

Obstruction of a major bronchus is invariably followed by collapse of the lung distal to the point of obstruction Why? The answer is based on the laws governing gas absorption from any air pocket in the body and is in the last analysis related to the shape of the oxygen dissociation curve of hemoglobin One result of this curve is the fact that the passage of oxygen from arterial blood to the systemic tissues is accompanied by a large drop of the partial pressure of oxygen in the blood The increase of partial pressure due to ad dition of carbon dioxide to the blood from the tissues is much less Nitrogen exerts virtually the same partial pressure in venous as in arterial blood The net result is that venous blood contains a total

pressure of gases which is less than the total pressure of gases in arterial blood which equals the atmospheric pressure minus the vapor pressure of water

Consider a pocket of air trapped in lung distal to an occluded bronchus At the start this gas has the same composition as alveolar air the partial pressure of oxygen is 100 mm Hg of CO_2 40 mm Hg and of nitrogen (if the barometric pressure is 747 mm Hg) 560 mm Hg Mixed venous blood containing oxygen at a partial pres sure of 40 mm Hg CO_2 at a pressure of 45 mm Hg and nitrogen at a pressure of 560 mm Hg comes into equilibrium with this gas A good deal of oxygen diffuses out of the pocket whereas a much smaller amount of CO_2 diffuses in until the partial pressures of these two gases in the pocket approaches that in the venous blood Since the oxygen loss is greater than the CO_2 gain the pocket becomes smaller At the same time the partial pressure of nitrogen rises be cause the total pressure in the pocket remains atmospheric This means that nitrogen will now diffuse out of the pocket resulting in an increase of the pressures of the other two gases and further reduction of the size of the pocket This sequence of events is repeated until the gas disappears and the lung collapses

PHYSIOLOGICAL COMPENSATIONS

COLLATERAL VENTILATION An interesting aspect of atelectasis is the fact that obstruction of small bronchi is not necessarily followed by lung collapse because some air passes through the pores of Cohn into the alveoli distal to the obstruction from adjacent ven tilated alveoli Since this collateral ventilation cannot occur between lobes atelectasis always follows obstruction of lobar bronchi Why does atelectasis ever develop after bronchiolar obstruction? One theory relates such atelectasis a frequent complication of surgery to the fact that a histamine like substance liberated by surgical trauma or by diseased tissues causes occlusion of the pores of Cohn so that when a bronchiole becomes obstructed atelectasis develops It has been suggested that antihistaminic drugs might prevent this com plication

REDUCED CIRCULATION Major atelectasis may be accompanied by little if any hypoxemia This indicates that the unventilated lung is not perfused with blood Prompt decrease of circulation to atelectatic

lung has been demonstrated experimentally Whether this is the result of mechanical collapse of blood vessels or of anoxia induced vaso constriction remains to be determined In favor of the mechanical explanation is the experimental observation that collapse of the isolated, perfused lung is accompanied by an increase of the vascular resistance Although atelectasis has little deleterious effect on mean arterial blood gas composition it should be treated in order to restore functioning lung tissue to obviate the development of infection and to reduce the work of the right ventricle

TREATMENT

The treatment of atelectasis is rendered difficult by the fact that the surface tension exerted by collapsed lung tissue is large Whereas 4 mm Hg serve to inflate normal lung from the end expiratory position 20 mm Hg or more of airway pressure are needed to over come this surface tension and to inflate atelectactic lung This is well known to the anesthesiologist who must apply large amounts of pressure to the airway in order to inflate atelectatic lung after thoracic surgery Such pressure may be dangerous, it may cause rupture of normal alveoli distal to unobstructed airways

Every effort should be made to prevent atelectasis in patients in whom it is apt to develop postoperative patients those in respirators, and otherwise immobilized cases Preventive measures include fre quent coughs and/or deep breaths and if necesary, tracheal aspira tion The use of antihistaminic drugs has been mentioned Inspiration of 100% oxygen should be avoided since oxygen filled alveoli col lapse much more readily than air filled alveoli (see below)

PNEUMOTHORAX

GAS ABSORPTION FROM AN AIR POCKET

A pneumothorax pocket is generally made up of room air at the start The laws governing its eventual absorption are similar to those outlined above for absorption of a pocket of gas trapped distal to an occluded bronchus Since the total pressure of gases in venous capillary blood is subatmospheric gas transfer continuously takes place from the pneumothorax into the blood until the pocket dis appears This process can be greatly accelerated by having the patient breathe oxygen just as the rate of development of atelectasis can be

speeded by having an animal breathe oxygen During oxygen breathing nitrogen is almost entirely displaced from the circulating blood and most of the total atmospheric pressure of gases in arterial blood is produced by oxygen Since some of this oxygen is dissolved in plasma release of normal amounts of oxygen to the tissues is accompanied by a tremendous drop of oxygen tension so that venous blood contains oxygen at a partial pressure of considerably less than 100 mm Hg The total pressure of gases in venous blood may be 120 mm Hg or less As a result the nitrogen in a pneumothorax pocket in which the pressure is atmospheric diffuses into the blood stream at a very rapid rate This principle has been utilized to combat abdominal distention by oxygen breathing as well as to hasten gas absorption from a pneumothorax pocket

The life of an artifically induced gas pocket such as pneumothorax or pneumoperitoneum depends upon the nature of the gas used Oxygen will be absorbed much more rapidly than nitrogen The recently developed synthetic gas sodium hexafluoride (SF_6) is of higher molecular weight and low solubility in tissue fluids As a result it is absorbed very slowly and should be useful for the maintenance of therapeutic pneumothorax or pneumoperitoneum

EFFECT ON LUNG VOLUME

Although pneumothorax is seldom used today for the treatment of tuberculosis the mechanics of lung collapse are still of interest The normal negative intrapleural pressure is the result of the elastic pull of the lung inward and of the chest wall outward If one allows air to enter between the lungs and the chest the chest will enlarge and the lungs will get smaller Actually the pressure volume characteristics of the lungs and chest are such that a given amount of air will be about equally divided into that taken up by lung collapse and that taken up by chest expansion Thus the introduction of 1000 cc of air into the chest causes the lungs to become about 500 cc smaller while the chest becomes about 500 cc larger

EFFECT ON PULMONARY FUNCTION

As in atelectasis blood flow to a lung collapsed by pneumothorax is reduced and so hypoxemia may not be present On the other hand partial lung collapse causes inequality of ventilation and perfusion in the lung with the result that the arterial oxygen saturation may be

reduced (Chap 11) Generally, hypoxemia is not a problem and functional limitation results only if the contralateral lung is inadequate to support total ventilation and perfusion (Chap 9 Resection of Lung Tissue)

ARTIFICIAL RESPIRATION

ACUTE

The technique of artificial respiration should be as familiar to physicians as it is to Boy Scouts No emergency requires more prompt and trained action than does apnea The goal of artificial respiration acute or chronic is to move the required volume of air into and out of the alveoli This requirement as outlined in Chapter 1, is dictated by the metabolic level of the tissues The volume of air moving in and out of the lung must equal the alveolar ventilatory requirement plus the volume that moves in and out of the tracheobronchial tree In administering chronic artificial respiration these principles are utilized One calculates the alveolar ventilatory requirements, adds the amount of air assumed or computed to move in and out of the dead space and sets the respirator to provide this total ventilation In an acute emergency one makes no such calculation but simply employs a technique known to be adequate The best technique is mouth to mouth breathing during which the operator inflates the patient's lungs with his own expired air His ventilation becomes that of his subject and the small amount of carbon dioxide in his expired air does not render the technique inadequate Every physician should become familiar with this technique which is the first step in resuscitation following cardiac arrest, drowning and other emergencies

CHRONIC

Pressure Breathing and Ventilatory Requirements

The proper administration of chronic artificial respiration is based on two principles (1) maintenance of a clear airway and (2) delivery of the required volume of air into and out of the alveoli without frustration of the patient's own respiratory efforts Air can be moved into the chest equally well by applying positive pressure at the mouth as by applying negative pressure around the chest as with a tank respirator The dynamics of the flow of air into and out

of the lungs are identical in the two situations In addition positive inspiratory pressure at the mouth produces effects on the circulation similar to those produced by a respirator which generates negative pressure around the body during inspiration With each device the intrapulmonary pressure during inspiration is *positive* relative to the venous pressure in the vena cavae This is intuitively obvious in the case of positive pressure at the mouth but not so clear in the case of the respirator In the latter inspiration is accompanied by a decrease of the pressure all around the body which serves to enlarge the chest and thus to draw air into the lungs The pressure in the body including the vena cavae, is also negative The flow of air into the lung causes the intrathoracic pressure to rise so that it becomes positive relative to the negative pressure in the rest of the body This causes relative obstruction of venous return to the chest For this reason some expiratory positive pressure in the respirator has been advocated to counteract the adverse circulatory effects of negative inspiratory pressure In general this is only necessary in individuals with impaired circulation in whom negative pressure breathing alone may lead to a drop of blood pressure and even to shock

A cuirass type respirator with only a negative phase has quite different effects With this device the thorax is subjected to negative pressure during inspiration but the abdomen which is outside the respirator remains at atmospheric pressure As a result the abdominal pressure is higher than the intrathoracic pressure throughout inspiration This type of respirator promotes venous return to the thorax during inspiration in contrast to a body respirator, and to inspiratory positive pressure at the mouth

As mentioned the respirator should be set so that the ventilation is maintained at the desired level The steps involved in regulation of the respirator settings are as follows Let us assume that the respirator will be set to cycle 10 times per minute A slow frequency of respiration minimizes the volume of air that goes in and out of the dead space and hence the total ventilatory requirements Furthermore at slow rates of ventilation the dead space takes up less of the tidal volume than at fast rates and any erroneous assumption of the size of the dead space results in less abnormality of the arterial P_{co} than would occur at fast respiratory rates Assuming that the lung dead space in cubic centimeters equals the weight in pounds in a 200 pound man 200 cc of air will go in and out of the dead

space with each breath, and the total dead space ventilation will be 2 0 liters per minute If one calculates, on the basis of normal standards for metabolic rate with suitable correction for fever that the alveolar ventilatory requirements are 4 0 liters per minute the patient requires 6 0 liters of ventilation Each breath must equal 600 cc The respirator is then set to give this tidal volume as registered on a spirometer or flow meter These calculations and as sumptions must be checked periodically by measurement of the alveolar or arterial P_{CO} and any deviation of this from 40 mm Hg must be corrected by appropriate increase or decrease of the tidal volume One ingenious method of accomplishing this task is to employ a servomechanism which consists of a continuous alveolar CO_2 analyzer which activates the respirator When the P_{CO_2} exceeds 40 mm Hg the respirator activity increases and a decrease of the P_{CO_2} causes a decrease of the respirator activity

Since most diseases that require artificial respirator therapy par ticularly poliomyelitis are associated with a reduction of the com pliance of the lung and/or chest wall larger amounts of pressure are required to produce normal tidal volumes than in normal subjects One explanation for this reduced compliance is that some areas of lung become atelectatic with the result that the amount of ventilated lung tissue is reduced Atelectasis may be prevented by periodic institution of deep breaths either by a sudden increase of the negative respirator pressure or by mechanical exsufflation at the mouth and there is some evidence that the reduction of compliance may be pre vented by such therapy

Respiratory Therapy

It is frequently difficult to know whether or not a respirator is necessary particularly in poliomyelitis Apprehension suggests the presence of alveolar hypoventilation and this may be confirmed by arterial blood gas analysis Fatigue is an indication for providing respirator assistance Measurement of the vital capacity is also helpful When this falls to less than 50 per cent of normal a respirator is probably indicated By the same token, improvement of the vital capacity is an indication that the patient can be removed from the respirator Ventilatory assistance is necessary until the vital capacity exceeds 30 per cent of normal

Weaning a patient from a respirator may be a difficult problem

Patients are often hyperventilated while in the respirator unless care fully regulated by measurement of the alveolar or arterial P_{CO_2} and they may have become accustomed to high levels of ventilation which they cannot maintain unaided If they do not maintain this ventilation the alveolar and arterial P_{CO_2} rise and the resultant acidosis may be intolerable These patients are particularly susceptible to the de velopment of acidosis since hyperventilation has led to reduced arterial P_{CO_2} which has been met by renal excretion of bicarbonate This means that the blood buffering power is reduced and so a de crease of ventilation results in a greater fall of blood pH than occurs in normals This is similar to the reduction of breath holding time which persists when the individual acclimatized to high altitude returns to sea level He too has lost buffer base secondary to hyper ventilation and is more affected by CO_2 retention during breath holding than is a person residing at sea level Periodic deep breaths may cut down the respirator patient s subjective ventilatory require ments by providing a subtsitute for the sighs and yawns which occur in the normal subject and which may be necessary in order to prevent reflex tachypnea from areas of lung which otherwise would not be come distended Ventilation may then be kept down to a normal level and subsequent removal from the respirator will be easier

Other Ventilatory Aids

Other ventilatory aids may be of value in chronic artificial respira tion One of these *is a rocking bed This operates on the principle* that in the feet down position gravity causes descent of the dia phragm and lung expansion This is followed by elevation of the diaphragm when the body is rotated to the head down position

Electrophrenic respiration is an interesting type of artificial respira tion When the phrenic nerve is intact as in poliomyelitis it may be stimulated electrically thereby causing diaphragmatic contractions and adequate ventilation This stimulation may be given through the skin or the electrode may be surgically implanted on the phrenic nerve

Recently, it has been found that patients may be taught to use the muscles of the glossopharynx to swallow air into the lung This frog breathing may actually result in sufficient alveolar ventilation to meet the resting requirements

REFERENCES

PULMONARY EDEMA

AVIADO D M and SCHMIDT C F Respiratory burns with special reference to pulmonary edema and congestion *Circulation 6* 666 1952

DRINKER C K and HARDENBERGH E Acute effects upon the lungs of large intravenous doses of alphanaphthyl thiourea (ANTU) *Am J Physiol 156* 35 1949

HENNEMAN P H Acute pulmonary edema with special reference to experimental studies *New England J Med 235* 590 1946

SARNOFF S J BERGLUND E and SARNOFF L C Neurohemodynamics of pulmonary edema III Estimated changes in pulmonary blood volume accompanying systemic vasoconstriction and vasodilation *J Appl Physiol 5* 367 1953

SHARP J T GRIFFITH G T BUNNELL I L and GREENE D G Ventilatory mechanics in pulmonary edema in man *J Clin Invest 37* 111 1958

VITALE A. DUMKE P R and COMROE J H JR Lack of correlation between rales and arterial oxygen saturation in patients with pulmonary congestion and edema *Circulation 10* 81 1954

WILLIAMS M H JR Effect of ANTU induced pulmonary edema on the alveolar arterial oxygen pressure gradient in dogs *Am J Physiol 175* 84 1953

ATELECTASIS AND PNEUMOTHORAX

ALLEY R. D and LINDSKOG G E Pharmacologic factors influencing collateral respiration possible relation to the etiology of pulmonary complications *Ann Surg 128* 497 1948

BJORK V O Circulation through an atelectatic lung in man *J Thoracic Surg 26* 533 1953

DALE W A and RAHN H Rate of gas absorption during atelectasis *Am J Physiol 170* 606 1952

DALE W A and RAHN H Experimental pulmonary atelectasis Changes in chest mechanics following block of one lung *J Appl Physiol 9* 359 1956

LINDSKOG G E Collateral respiration in the normal and diseased lung *Yale J Biol & Med 23* 311 1951

PETERS R. M and ROOS A The effects of atelectasis on pulmonary blood flow in the dog *J Thoracic Surg 24* 389 1952

ROSENBERG M A Effects of unilateral collapse of the lung *Yale J Biol & Med 25* 51 1952

SWALBACH W G SCHWARTZ S I RAHN H and HODGE H C Use of a new gas sulfur hexafluoride SF in pneumoperitoneum *Am Rev Tuberc & Pulmonary Diseases 76* 1063 1957

TENNEY S M CARPENTER F G and RAHN H Gas transfers in a sulfur hexafluoride pneumoperitoneum *J Appl Physiol 6* 201 1953

WILLIAMS M H JR The alveolar arterial oxygen tension difference in open chest dogs *Am J Physiol 184* 109 1956

ARTIFICIAL RESPIRATION

AARSVOLD C M Artificial ventilation in poliomyelitis *J Oslo City Hosp 4* 153 1954

COLLIER C R and AFFELDT J E Ventilatory efficiency of the cuirass respirator in totally paralyzed chronic poliomyelitis patients *J Appl Physiol 6* 531 1954

COLLIER C R DAIL C W and AFFELDT J E Mechanics of glossopharyngeal breathing *J Appl Physiol 8* 580 1956

DILL, D B Ed Symposium on mouth to mouth resuscitation (expired air inflation) *J.A.M.A 167* 317 1958

FERRIS B G JR WARREN A and BEALS C A Vital capacity as a measure of spontaneous breathing ability in poliomyelitis *New England J Med 252* 618 1955

LUKAS D S and PLUM F Pulmonary function in patients convalescing from acute poliomyelitis with respiratory paralysis *Am J Med 12* 388 1952

RADFORD E P JR FERRIS B G JR and KRIETE B C Clinical use of a nomogram to estimate proper ventilation during artificial respiration *New England J Med 251* 877 1954

SAXTON G A JR and MYERS G A servomechanism for automatic regulation of pulmonary ventilation *J Appl Physiol 11* 326 1957

WHITTENBERGER J L SARNOFF S J and HARDENBERGH E Electrophrenic respiration II Its use in man *J Clin Invest 28* 124 1949

WHITTENBERGER J L Artificial respiration *Physiol Rev 35* 611 1955

WHITTENBERGER, J L and FERRIS B G JR Alterations of respiratory function in poliomyelitis *Am J Phys Med 31* 226 1952

CHAPTER 11

HYPOXIA, HYPOXEMIA, AND CYANOSIS

HYPOXIA

Hypoxia may be defined as a condition of inadequate availability of oxygen for cell function It is most commonly due to reduced supply of oxygen to the tissues This, in turn may result from decreased arterial oxygen content, hypoxemia or from impaired circulation general or systemic Poisoning of oxidative enzyme systems histotoxic hypoxia such as occurs in cyanide poisoning is not due to diminished tissue oxygen supply and will not be discussed here The term *hypoxia* is used in preference *to anoxia* to denote a relative rather than an absolute oxygen lack

PATHOGENESIS

Tissue hypoxia is present when the supply of oxygen to the tissues is inadequate to meet the demands for tissue oxygen consumption Oxygen supply to the tissues depends upon the arterial oxygen content and upon the amount of blood flowing to the tissues Arterial oxygen content depends upon the amount of hemoglobin present in the blood and upon the degree to which that hemoglobin is saturated with oxygen the arterial oxygen saturation Subnormal amounts of hemoglobin in the blood reduced arterial oxygen saturation or decreased blood flow to the tissues may all lead to hypoxia, particularly if the metabolic activity, or oxygen uptake of the tissues is increased

In hypoxia subnormal amounts of oxygen are brought to the tissues and the tissues extract increased amounts of oxygen from the blood that is brought to them This leads to an abnormal reduction of the oxygen saturation of the blood leaving the tissues A low venous oxygen saturation is probably the best indication that hypoxia is present

SYMPTOMS

Systemic hypoxia is associated with surprisingly few symptoms The aviator at 40 000 feet whose oxygen supply suddenly becomes defective may experience some blurring of sensibility and some euphoria but he rapidly loses consciousness and dies before un pleasant warning symptoms can make their appearance The mild hyperventilation associated with hypoxia causes insufficient increase of respiratory work to be experienced as dyspnea (Chap 12)

Local hypoxia may be associated with specific symptoms angina pectoris results from myocardial hypoxia intermittent claudication from hypoxia of the exercising limbs Other organs may suffer im pairment of function without giving rise to symptoms and it is important to prevent and to correct local hypoxia just as it is essential to prevent severe systemic hypoxia if life is to be maintained

HYPOXEMIA

Hypoxemia is defined as a condition in which there are subnormal amounts of oxygen in the arterial blood It may be the result of (1) environmental factors if the oxygen tension of the inspired air is re duced (2) pulmonary disease which causes impaired ventilation diffusion or distribution of gases (3) intracardiac or intrapulmonary right to left shunts or (4) reduced or altered oxygen carrying power of the blood Understanding of the pathophysiology of each of these situations enables the physician to detect and to quantitate the type of abnormality responsible for hypoxemia and to apply the proper ther apy In addition such understanding provides the physician with in sight into the degree to which cardiopulmonary function has been altered in a given patient This in turn has prognostic importance and is of diagnostic value in that some information is available as to how much and what type of hypoxemia is present in many forms of cardiopulmonary disease The various types of hypoxemia will be dis cussed the physiological diagnosis of each type will be outlined and certain diagnostic therapeutic and prognostic implications will be mentioned Table 4 provides a classification of pulmonary disease in terms of the various types of functional impairment and of the asso ciated abnormalities of arterial blood gas composition

TABLE 4 CLASSIFICATION OF PULMONARY DISEASE IN TERMS OF FUNCTIONAL IMPAIRMENT AND ABNORMALITY OF ARTERIAL BLOOD GASES

Functional impairment	*Disease*	*Physiological abnormality*
Hypoventilation from		
Depression of respiratory center	Emphysema	Acidosis CO_2 retention if severe hypoxemia relieved by oxygen
Muscle paralysis	Polio	
Airway obstruction	Asthma emphysema	
Decreased compliance	Fibrosis pulmonary edema	
Impaired diffusion from		
Loss of alveolar capillary surface	Resection emboli emphysema	Hypoxemia aggravated by exercise relieved by oxygen no CO_2 retention
Thickening of alveolar walls	Fibrosis	
Impaired distribution from		
Effective right to left shunt	Pulmonary arterio venous fistula atelectasis pulmo nary edema	Hypoxemia unrelieved by oxygen no CO_2 retention
Uneven ventilation and perfusion	Lung collapse emphysema	Hypoxemia largely relieved by oxygen moderate CO_2 retention

DIMINISHED ALVEOLAR OXYGEN TENSION

Diminished Inspired Oxygen Tension

The first factor in the oxygenation of the blood is the alveolar oxygen tension The arterial oxygen tension can be no higher than the alveolar oxygen tension If the alveolar oxygen tension is reduced hypoxemia has to result This happens when the inspired oxygen tension is reduced as at high altitudes or during the inspiration of low oxygen mixtures Under these circumstances the partial pressure of inspired oxygen is reduced and so there is a corresponding reduc tion of the partial pressure of oxygen in the alveoli and in the arterial blood When the arterial oxygen tension is reduced, the arterial oxygen saturation falls The degree of hypoxemia is dependent upon the degree of reduction of the inspired oxygen tension

Diminished Alveolar Ventilation

Clinically, reduced alveolar oxygen tension occurs when the alveolar ventilation is diminished relative to the metabolic rate or to

oxygen consumption The alveolar oxygen tension is directly proportional to the alveolar ventilation and inversely proportional to the oxygen consumption (Chap 1) If the alveolar ventilation is subnormal relative to the metabolic rate the alveolar oxygen tension is reduced This is accompanied by a corresponding increase of the alveolar carbon dioxide tension Actually carbon dioxide retention appears before significant hypoxemia because the flat portion of the oxygen dissociation curve of hemoglobin permits considerable reduction of the oxygen tension in blood before the oxygen saturation falls Hypoxemia due to alveolar hypoventilation is accompanied by relatively more carbon dioxide retention than hypoxemia due to the other types of abnormality

Alveolar hypoventilation most commonly occurs because of reduction of the total ventilation as in poliomyelitis It may also occur because of increased size of the lung dead space the passage through which air must pass to enter the alveoli Under these circumstances so much air is wasted going in and out of the dead space that subnormal quantities reach the alveoli In practice this situation is most commonly encountered during the administration of anesthetic agents through a large artificial dead space interposed between the patient s mouth and the breathing valve It also occurs among skin divers using snorkel gear Alveolar hypoventilation can be prevented if the tidal volume is increased by an amount equal to the volume of the added dead space

As discussed in Chapter 6 the work of breathing is so great in emphysema that the respiratory muscles use up large amounts of oxygen Increased ventilation may actually cause a greater increase of oxygen consumption by these muscles than of alveolar ventilation For example a doubling of alveolar ventilation may cause so much respiratory work that the oxygen consumption increases threefold Thus hyperventilation leads to relative alveolar hypoventilation so that the alveolar P_{CO} rises and the P_{O} falls

The proper treatment of hypoxemia due to alveolar hypoventilation is the augmentation of alveolar ventilation This may be achieved by removal of the underlying cause of alveolar ventilatory insufficiency as by the improvement of airway obstruction in pulmonary emphysema It may also be achieved by providing an increase of total ventilation either by stimulation of the respiratory center with drugs or by mechanical respiratory aids such as inspiratory positive pressure

breathing (IPPB) Advanced cases of alveolar ventilatory insufficiency require a respirator for adequate treatment As discussed in Chapter 10, the proper guide to the administration of artificial ventilation is the alveolar or arterial P_{CO} which should be kept at 40 mm Hg This is the end point of therapy of alveolar hypoventilation Although oxygen breathing will overcome the hypoxemia it does not directly affect the carbon dioxide retention This is apt to become worse after restoration of a normal arterial oxygen saturation removes the hypoxemic stimulus to the respiratory center

NORMAL ALVEOLAR DECREASED ARTERIAL OXYGEN TENSION

Hypoxemia may occur in the presence of normal ventilation and normal alveolar gas composition if there is some abnormality which prevents the arterial oxygen tension from attaining the same value as the alveolar oxygen tension This may take the form either of impairment of diffusion of oxygen across the alveolar membrane or of impairment of distribution of blood and gas in the lungs (or heart), so that some mixed venous blood reaches the arterial system without having been exposed to alveolar air

Impaired Diffusion

The diffusion of oxygen from the alveolar air into the capillary blood is dependent on physical laws As such its efficiency depends upon two characteristics of the surface across which the gas molecules diffuse its area and its permeability In the lung the diffusion surface is the entire area of the alveolar capillary membrane Impaired diffusion results from thickening of this membrane as in pulmonary fibrosis or from reduction of the area of the membrane as in emphysema

Diffusion may be assessed quantatively by measurement of the diffusing capacity of the lung This is a measure of the thinness and of the size of the alveolar capillary surface An indication of severe impairment of diffusion may be suggested by arterial blood gas analysis If the diffusion surface is greatly thickened or destroyed oxygen traverses the alveolar-capillary membrane at such a slow rate that the blood leaving the alveolar capillaries contains subnormal quantities of oxygen The hypoxemia due to impaired diffusion has two characteristics it is greatly accentuated by muscular exercise and it is overcome by oxygen breathing As regards the former in

creased oxygen consumption places such a great demand on a limited diffusion surface that the arterial oxygen saturation falls precipitously On the other hand elevation of the alveolar oxygen tension by oxygen breathing causes oxygen to diffuse across the alveolar membrane so rapidly that hypoxemia is abolished Since carbon dioxide is over twenty times as 'diffusible as oxygen, carbon dioxide retention is rarely if ever an accompaniment of hypoxemia due to an uncomplicated diffusion limitation

The normal alveolar capillary membrane is so large and so thin and oxygen diffuses into the blood flowing through the alveolar capillaries at such a rapid rate that the blood becomes fully saturated with oxygen before it reaches the end of the alveolar capillary Most of the oxygen transfer from alveolus to blood takes place at the beginning of the normal alveolar capillary and the partial pressure of oxygen in the alveolar capillary blood becomes identical to the alveolar oxygen tension before the blood reaches the end of the alveolar capillary (Chap 1) This means that diffusion must become greatly impaired before the oxygen tension in the blood leaving the alveolar capillaries falls lower than the oxygen tension in the alveoli Diffusion is seldom so badly impaired that a reduced diffusing capacity is the sole cause of hypoxemia However, once diffusion is so limited that hypoxemia is present further impairment leads to a precipitous fall of the arterial oxygen saturation

Hypoxemia due to impaired diffusion is a poor prognostic sign It means that there is considerable thickening or destruction of the alveoli *and the hypoxemia will become more severe if the underlying* disease gets worse Patients with such a limitation may expect marked improvement from oxygen breathing On the other hand, they must be cautioned against placing any great strain on the diffusion process by indulging in heavy exercise or by ascending to high altitudes Every effort must be made to prevent progression of the underlying disease so as to prevent a progressive fall of the arterial oxygen saturation

Impaired Distribution

RIGHT TO LEFT SHUNTS The other general situation in which hypoxemia exists because of a difference between the alveolar and arterial oxygen tensions is impaired distribution of blood and gas in the lung The most extreme form of this is a right to left shunt In this condition venous blood having bypassed the lung and therefore

having a low oxygen saturation, mixes with the fully saturated blood which has passed through the alveolar capillaries The resultant mixture the arterial blood, has an oxygen saturation which is somewhere between that of its two components If the shunt is small the arterial oxygen saturation is similar to the saturation of the blood leaving the alveolar capillaries If the shunt is large the arterial saturation is more like that of the mixed venous blood Thus, the degree of hypoxemia depends upon the oxygen saturation of the blood leaving the alveolar capillaries the oxygen saturation of the mixed venous blood and the relative magnitude of the shunt If cardiopulmonary function is normal, the blood leaving the alveolar capillaries may be assumed to be 97 per cent saturated with oxygen and the mixed venous blood to have an oxygen saturation about 25 per cent less than the arterial oxygen saturation Under these circumstances analysis of the arterial oxygen saturation provides quantitative information about the magnitude of the right to left shunt since the degree of hypoxemia is largely dependent upon the amount of blood flowing through the shunt as compared to the amount of blood not flowing through the shunt Ordinarily hypoxemia is not detectable until there is a shunt of 25 per cent or more of the total cardiac output

Hypoxemia of this type is only partially relieved by oxygen breathing The inspiration of 100 per cent oxygen elevates the oxygen tension in the alveoli to about 670 mm Hg A little oxygen becomes dissolved in the blood flowing through these alveoli but the hemoglobin was already almost fully saturated with oxygen and so the gain is slight It amounts to approximately 2 volumes per cent the equivalent of about 10 per cent oxygen saturation Since the oxygen saturation of the two components of the arterial blood is raised a little bit by oxygen breathing the arterial oxygen saturation also rises One can anticipate that the arterial oxygen saturation will rise about 10 per cent when the patient breathes oxygen A larger increase of the arterial oxygen saturation suggests either that some other mechanism was entirely or in part responsible for the hypoxemia or that the proportion of the right ventricular output flowing through the shunt became less during oxygen breathing This may occur in certain patients with congenital heart disease and pulmonary vasoconstriction (Chap 3)

Hypoxemia is present in patients with right to left shunts because the venous oxygen saturation is so much lower than the oxygen satura

tion of the blood leaving the alveolar capillaries The carbon dioxide content of venous blood is only a little bit higher than the carbon dioxide content of blood leaving the alveolar capillaries and thus significant carbon dioxide retention seldom accompanies this type of hypoxemia

Anatomical right to left shunts cardiac and pulmonary have been discussed in Chapter 2 Atelectasis and other types of pulmonary disease in which the alveoli are perfused with blood but not ventilated also cause effective right to left shunts Under these circumstances venous blood passes through some sections of the lung without taking up any oxygen and mixes with the blood leaving the normal alveolar capillaries to cause reduction of the arterial oxygen saturation The degree of hypoxemia is a measure of the size of the shunt and hence of the severity of the existing pulmonary disease It is of interest that extensive pulmonary disease is often associated with surprisingly little hypoxemia This is due to the fact that collapse or infiltration of lung tissue usually causes obliteration of capillaries as well as of alveoli As a result the nonventilated areas are no longer perfused with blood In addition as discussed in Chapter 1 it is possible that a decrease of the alveolar oxygen tension leads to pulmonary vasoconstriction so that right to left shunts through hypoxic alveoli are prevented

UNEVEN VENTILATION AND PERFUSION A more subtle form of hypoxemia due to impaired distribution results from diminution of ventilation without compensatory reduction of the circulation to some areas of lung In hypoventilated alveoli the oxygen tension falls with the result that the blood leaving these alveoli has a reduced oxygen saturation If this is accompanied by hyperventilation of other alveoli the mixture of alveolar air from all of the alveoli may be normal Hypoxemia is present because the hyperventilated alveoli contribute blood which is very little raised in oxygen saturation since the blood that leaves normally ventilated alveoli is almost fully saturated with oxygen Increase of the alveolar oxygen tension above 100 mm Hg does not cause a corresponding increase of the oxygen saturation of the blood Thus the low saturation blood from poorly ventilated alveoli mixes with normally saturated blood from hyperventilated alveoli Hypoxemia results

This situation is generally accompanied by some carbon dioxide

retention It is completely relieved by oxygen breathing unless there are some areas of functional shunt completely nonventilated alveoli. If any air gets into the alveoli at all inspiration of oxygen will elevate the alveolar oxygen tension to well above 100 mm Hg and thus provide complete saturation of the blood flowing through these alveoli *This type of hypoxemia is also treated by measures which improve* the intrapulmonary distribution of inspired air so that all of the alveoli receive similar amounts of ventilation Such measures include bronchodilators IPPB, and elimination of infection in the tracheo bronchial tree

NORMAL ARTERIAL OXYGEN TENSION DIMINISHED OXYGEN CONTENT

Hypoxemia occurs despite a normal arterial oxygen tension in the blood when the oxygen combining power of the blood is reduced This happens in anemia when there are decreased amounts of hemo globin present for combination with oxygen, and in situations in which certain abnormal types of hemoglobin are present in the blood When pigments such as methemoglobin and carbon monoxide hemo globin replace the normal hemoglobin in the blood, there is a dimin ished quantity of the latter available for combination with oxygen

Carbon Monoxide Poisoning

Inspiration of low concentrations of carbon monoxide is harmful because carbon monoxide has a much greater affinity for *hemoglobin* than does oxygen Even when the partial pressure of carbon monoxide in the alveoli is much lower than that of oxygen, most of the hemo globin becomes bound by carbon monoxide In addition carbon monoxide hemoglobin appears to have the unique property of pre venting dissociation of oxyhemoglobin and so oxygen is not released to the tissues Treatment is elevation of the alveolar oxygen tension and reduction of the alveolar carbon monoxide tension so that oxy hemoglobin will be formed and carbon monoxide hemoglobin decreased This is accomplished by inhalation of oxygen, with artificial ventilation if necessary

IMPAIRED CIRCULATION—STAGNANT HYPOXIA

Arterial oxygen tension and content may be normal but tissue hypoxia still occurs if inadequate amounts of blood reach the tissues

relative to metabolic needs In occlusive peripheral arterial disease or when the cardiac output is reduced, the blood flows through the tissues very slowly The cells extract so much oxygen from the blood that the oxygen tension drops to very low levels before the blood reaches the end of the capillary As a result some of the cells are exposed to blood containing oxygen at a very low tension Oxygen cannot diffuse into these cells at sufficiently rapid rate to meet meta bolic needs The functional consequences are different for each organ and the degree of impairment depends upon the metabolic rate and the blood supply to the organ

Treatment of hypoxia of this type depends upon improvement of the circulation If systemic blood flow is reduced hypoxia may be corrected by measures aimed at improving cardiac function (Chap 4) Hypoxia due to arterial obstruction may be relieved by sympa thetic block chemical or surgical or by reconstructive vascular surgery Very little is achieved by treating this type of hypoxia by inhalation of oxygen (Chap 5 Ischemic Heart Disease)

CYANOSIS

Cyanosis is not synonymous with hypoxemia, although reduced arterial oxygen saturation is one cause of cyanosis Cyanosis is present when there are abnormally large amounts of reduced hemoglobin in the systemic capillaries Its intensity depends upon the amount of hemoglobin present in the blood the red cell concentration and upon the average oxygen saturation of the blood flowing through the skin capillaries The latter depends upon the oxygen saturation of the blood entering the capillaries the arterial oxygen saturation and upon the amount of oxygen extracted from the blood as it traverses the capillary The lower the arterial oxygen saturation and the greater the extraction of oxygen from each unit of blood the lower the mean capillary oxygen saturation will be The rate of extraction of blood from the capillaries depends upon the metabolic rate of the tissues and upon the magnitude of the blood flow More oxygen is extracted if the metabolic rate is high than if it is low and more oxygen is ex tracted from each unit of blood if the total amount of blood flow to the tissues is reduced The intensity of cyanosis then is related to the hematocrit to the arterial oxygen saturation to the skin oxygen consumption and to the amount of blood flow through the skin

The intensity of cyanosis is also dependent upon the structure of the skin, the ease with which the dark pigment in the capillaries is visible to the observer It is not surprising that cyanosis is unreliable as a clinical sign of hypoxemia and that the correlation between cyanosis and the arterial oxygen saturation is poor In an individual

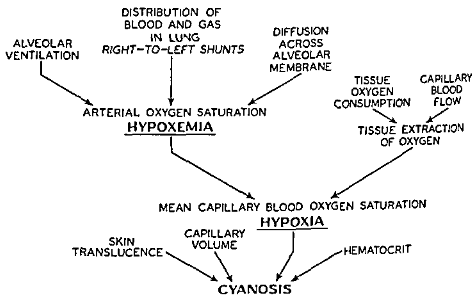


Fig 23 Schematic summary of the relationships between hypoxemia hypoxia and cyanosis Hypoxemia may result from reduced alveolar ventilation impaired distribution of blood and gas in the lung or impaired diffusion across the alveolar capillary membrane Either hypoxemia or increased extraction of oxygen by the tissues may lead to reduced oxygen saturation of the blood flowing through the capillaries hypoxia which is a major cause of cyanosis

with normal skin and hematocrit cyanosis is only evident when the arterial oxygen saturation is lower than 85 per cent An elderly thin skinned individual may appear cyanotic when the arterial oxygen saturation is normal Proper evaluation of hypoxemia requires arterial blood gas analysis and the absence of cyanosis is no assurance that the arterial oxygen saturation is normal

POLYCYTHEMIA

Polycythemia is an important complication of hypoxemia Direct or humoral stimulation of the bone marrow by lowered arterial oxygen saturation causes an increased production of red blood cells in direct

proportion to the degree of hypoxemia Natives residing at an altitude of one mile in Denver have slight but definite polycythemia by sea level standards and this becomes increasingly severe in populations living at higher altitudes

Polycythemia appears to be a compensatory adjustment to prevent tissue hypoxia It causes increased oxygen carrying power of the blood and hence increased oxygen supply to the tissues When polycythemia becomes severe, however it may be deleterious in that the increased viscosity of the blood causes an increased resistance to blood flow For this reason particularly in the presence of heart failure phlebotomy is advised if the hematocrit becomes very high

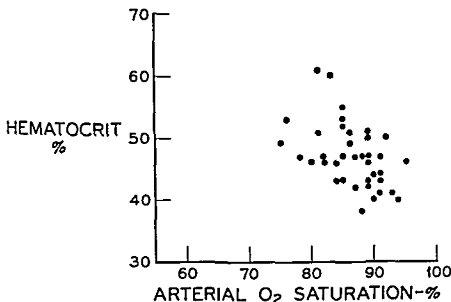


Fig 24 Relationship between the hematocrit and the arterial oxygen saturation in 22 patients with pulmonary emphysema many of whom were studied repeatedly Severe polycythemia always accompanied by hypoxemia but mild degrees of polycythemia may be associated with a normal arterial oxygen saturation and mild hypoxemia need not cause polycythemia

This is true both in congenital heart disease (Chap 3) and in pulmonary disease The optimal degree of polycythemia in either situation is not known but in pulmonary emphysema it is customary to keep the hematocrit below 60 per cent in order to prevent the development of right heart failure

Polycythemia vera is a primary disease of the bone marrow Dis

tinction between primary and secondary polycythemia is generally provided by measurement of the arterial oxygen saturation In congenital heart disease, severe polycythemia is always accompanied by severe hypoxemia If the hematocrit is over 50 because of pulmonary disease the arterial oxygen saturation is generally less than 90 per cent (Fig 24) On the other hand milder degrees of polycythemia may be present when the arterial oxygen saturation is nearly normal and so differentiation of such cases from mild polycythemia vera may be difficult This is complicated by the fact that polycythemia vera may cause reduction of the arterial oxygen saturation to levels as low as 90 per cent because of secondary effects on the lungs On the other hand if one can make a definitive diagnosis of a disorder which could lead to hypoxemia secondary polycythemia is probably present

REFERENCES

BARTELS S *et al* Determination of shunted blood and of the diffusion capacity of the lung in health and in pulmonary disease *Arch ges Physiol 261* 99 1955

BERGGREN S M The oxygen deficit of arterial blood caused by nonventilating parts of the lung *Acta physiol scandinav 4* Suppl XI 92 1942

DONALD K W RENZETTI A RILEY R L and COURNAND A Analysis of factors affecting concentrations of oxygen and carbon dioxide in gas and blood of lungs results *J Appl Physiol 4* 497 1952

FILLEY G F GREGOIRE F and WRIGHT G W Alveolar and arterial oxygen tensions and the significance of the alveolar arterial oxygen tension difference in normal men *J Clin Invest 33* 517 1954

HUSSON G and OTIS A B Adaptive value of respiratory adjustments to shunt hypoxia and to altitude hypoxia *J Clin Invest 36* 270 1957

LILLEHI J P JOHNSON R L WU N HALDEN E R and SPROULE B J Venous arterial admixture in the lungs in primary and secondary polycythemia *Circulation 17* 1029 1958

LUNDSGAARD C and VAN SLYKE D D Cyanosis *Medicine 2* 1 1923

PLATTS M M The arterial blood gases in pulmonary heart failure *Clin Sc 12* 63 1953

RATTO O BRISCOE W A MORTON J W and COMROE J H JR Anoxemia secondary to polycythemia and polycythemia secondary to anoxemia *Am J Med 19* 958 1955

SELZER A Chronic cyanosis *Am J Med 10* 334 1951

TINSLEY J C JR MOORE C V DUBACH R MINNICH V and GRINSTEIN M The role of oxygen in the regulation of erythropoiesis Depression of the rate of delivery of new red cells to the blood by high concentrations of inspired oxygen *J Clin Invest 28* 1544 1949

WASSERMAN L R ROBSON R L and LAWRENCE J H Blood oxygen studies in patient with polycythemia and in normal subjects *J Clin Invest* *28* 60 1949

WILLIAMS M H JR Quantitative relationships between hypoxemia and disorder of pulmonary function *Yale J Biol & Med* *30* 306 1958

CHAPTER 12

DYSPNEA

A common problem encountered by the practicing physician is that of the patient who complains of shortness of breath It is sometimes difficult to decide whether this symptom is the result of heart disease, lung disease or neither A variety of tests of cardio pulmonary function are useful in the evaluation of such a patient

THE NATURE OF DYSPNEA

Shortness of breath is a symptom and not an objective laboratory measurement Two patients with identical alteration of pulmonary or cardiac function may have very different complaints, an individual s subjective reaction to disease is of paramount importance in his description of his symptoms

It is not known whether dyspnea is a reflection of an individual s need for more ventilation perhaps because of oxygen lack excessive carbon dioxide in certain cells or discomfort induced by the increased work of breathing Since dyspnea often occurs in the absence of a demonstrable abnormality of the arterial blood gas composition it cannot be ascribed to hypoxemia or hypercapnia

If one runs upstairs dyspnea is not noticeable until one reaches the top of the stairs and starts to pant During the ascent dyspnea is usually not present This may result from the fact that the subject is distracted by his exertion and is not hyperventilating At the end of the climb, he breathes rapidly and deeply and becomes aware of shortness of breath

Although dyspnea is probably related to awareness of increased work of breathing other factors may be important For example it is not clear that the sensation of air hunger in the inadequately ventilated

respirator patient is true dyspnea Certainly feelings of suffocation and of apprehension accompanying the inability to breathe are factors which color and intensify dyspnea

By physiological study one may determine the presence or absence of some abnormalities which may make breathing difficult and lead to shortness of breath On the other hand it is impossible to state how much shortness of breath should be present in a given patient and what level of ventilation might be uncomfortable The following should be interpreted with this in mind

PATHOPHYSIOLOGY

Although there are no objective indexes of the presence and severity of dyspnea a good deal of information is available about the various types of abnormality of cardiopulmonary function that are encountered in patients who complain of it From this type of information it is possible to construct a hypothesis about the cause of dyspnea in terms of abnormal physiology and to outline the tests that are useful in defining whether or not such abnormalities are present in a given patient and whether or not they are sufficiently severe to cause dyspnea

INCREASED WORK OF BREATHING

Increased Intrathoracic Pressure Swing

It is not immediately apparent why disease of the heart should result in shortness of breath but it is becoming increasingly clear that dyspnea even in patients with heart disease is largely the result of abnormalities in the lung In heart disease these consist initially of pulmonary vascular engorgement and in advanced disease of actual change in the lung parenchyma i e pulmonary fibrosis Both processes cause increased lung stiffness and hence increased work of breathing since increased force must be applied to the lungs to produce a normal amount of ventilation Marshall and his collaborators have recently shown that when dyspnea occurs during heavy activity in normal subjects or during mild activity in patients with mitral stenosis there is one common denominator a large increase of the respiratory variation of intrathoracic pressure In both situations dyspnea appears when this pressure swing approaches 40 cm of water In the patient with mitral stenosis this happens at a low level

of activity and ventilation because the lungs are more resistant to stretch, whereas the normal individual only develops so large a respiratory variation of intrathoracic pressure during heavy activity The reality of dyspnea as a symptom of underlying disease may be determined by measuring the intrathoracic pressure during conditions when dyspnea is present This is easily done by passing a small tube into the esophagus for recording of the pressure fluctuations there a satisfactory index of intrapleural pressure change

Hyperventilation

Some types of lung disease lead to reflex hyperventilation which coupled with airway obstruction and/or decreased compliance adds to the work of breathing Pulmonary congestion either from mitral stenosis or left ventricular failure, is associated with reflex hyper ventilation, both during rest and exercise Tachypnea also occurs in pulmonary fibrosis and in pulmonary vascular disease Patients with these disorders hyperventilate at all levels of activity This coupled with the fact that each level of ventilation requires more than normal amounts of respiratory work because of parenchymal or airway abnormality results in dyspnea

HYPOXIA OF RESPIRATORY MUSCLES

Another aspect of this symptom is largely theoretical and concerns the oxygen supply to the respiratory muscles If one postulates that dyspnea is the result of nervous impulses from overworked respiratory muscles one might assume that reduction of the oxygen supply to these muscles might lead to the same symptom at a lower level of work This is entirely speculative but may explain the fact that dyspnea occurs in anemia and in some cases of heart failure when the work of breathing does not appear to be great The amount of oxygen brought to the respiratory muscles is dependent upon the blood flow to the muscles and upon the amount of oxygen in that blood Reduction of cardiac output of the oxygen combining power of the blood or of the arterial oxygen saturation might lead to dyspnea at a relatively low level of respiratory work These relationships are summarized schematically in Figure 25 The exact contribution of each to the development of dyspnea awaits the more precise delineation of this symptom and its neurophysiological basis

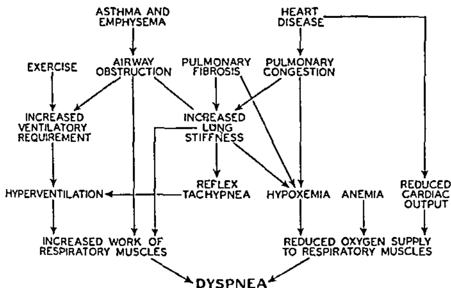


Fig 25 Schemat c summary of th facto s l ading to the de elopment of dyspnea In a ous typ s of card opulmo ary d sease It is based pon the hypothes s that dyspnea occurs when the e p atory m scles are forced to do more wo k than can be met by the r oxygen s pply

PHYSIOLOGICAL DIAGNOSIS OF THE CAUSE OF DYSPNEA

HEART DISEASE

With this as background it becomes pertinent to examine the various types of disease that cause dyspnea and to seek physiological clues to their presence

Cardiac disease apparently causes dyspnea because of secondary changes in the lung The first of these elevated pulmonary capillary pressure may be determined by cardiac catheterization (Chap 5) Increased pressure in the pulmonary capillaries causes transudation of fluid into the interstices of the lung This makes the lungs stiffer or less compliant and reduction of the lung compliance is found in patients with dyspnea due to heart disease A rough index of the extent of pulmonary congestion is the degree of reduction of the vital capacity Encroachment of fluid filled areas upon air containing lung causes reduction of all the subdivisions of lung volume of which the vital capacity is the most easily measured

Pulmonary congestion leads to reflex hyperventilation with the result that excessive amounts of carbon dioxide are blown off and the

arterial carbon dioxide tension is reduced both during rest and exercise The arterial oxygen saturation is generally normal or only slightly reduced, although severe pulmonary congestion, with pulmonary edema may lead to hypoxemia (Chap 10)

Another abnormality generally found when a cardiac patient reaches the point of complaining of dyspnea is reduction of the cardiac output In mild cases the cardiac output may be normal at rest but fail to rise normally during exercise This may be measured and compared to normal values for a given task A simpler and more generally available measurement is that of the pulse rate during rest and exercise Normally this increases 6 to 8 beats per minute for each 100 cc increase of oxygen consumption Patients with heart disease respond to a given task with a greater degree of tachycardia than normal subjects so that measurement of the heart rate during exercise, for which the oxygen consumption is either known or measured may be a useful guide to the presence or absence of heart disease as a cause of shortness of breath

Recently considerable attention has been given to the Valsalva maneuver as a test of cardiac function Normally if one raises the intrathoracic pressure to 30 to 40 mm Hg for 15 seconds by blowing against a mercury column the systolic blood pressure rises and then after 1 to 3 seconds of strain falls sharply to near control levels Upon release of the strain, there is a prompt fall to a subnormal pressure followed by an overshoot or rebound to a high level Patients with heart disease are characterized by absence of the first fall of pressure during continued strain and when the strain is released, by fall of the pressure to normal without a secondary rise The finding of such a response suggests that dyspnea is due to heart failure and a normal response tends to exclude cardiac disease as the cause of dyspnea

PULMONARY DISEASE

Pulmonary disease sufficient to cause shortness of breath may be divided into three categories restrictive obstructive, and vascular

Restrictive

Restrictive pulmonary disease the result of pulmonary fibrosis causes dyspnea both by reflex tachypnea and by decreased lung compliance This may be accompanied by surprisingly little abnormality

of ventilatory function, although there may be some reduction of the vital capacity. Because of the reflex tachypnea, the arterial carbon dioxide tension is reduced both during rest and exercise. The arterial oxygen saturation may be normal although in advanced cases hypoxemia, exaggerated by exercise and relieved by oxygen breathing, is found (Chap. 7). The diffusing capacity of the lung is generally reduced in patients who are short of breath because of pulmonary fibrosis, and this test may provide the only definite evidence of functional abnormality. Normally, during exercise, the diffusing capacity exceeds 25 cc. uptake of carbon monoxide per minute per millimeter Hg. Patients with severe dyspnea due to pulmonary fibrosis have values less than 10, whereas moderate dyspnea is associated with values between 10 and 25. A normal diffusing capacity excludes pulmonary fibrosis as the cause of shortness of breath.

Obstructive

Obstructive pulmonary disease (Chap. 6) causes dyspnea by increasing the work of moving air through the airways. This is accompanied by evidence of airway obstruction on spirometry. A convenient index of airway caliber is the maximal mid-expiratory flow rate (M.M.F.), which is the rate at which air is expired from the lungs during the mid-portion of a forced expiration. If the M.M.F. is greater than 1 liter per second, dyspnea due to obstructive pulmonary disease is unlikely, although patients with asthma may have a normal M.M.F. while in remission. Patients with dyspnea due to asthma or emphysema generally reveal moderate hypoxemia and CO_2 retention in the arterial blood. Exercise increases these abnormalities, and oxygen breathing overcomes the hypoxemia but may, as a result, lead to hypoventilation with further elevation of the arterial P_{CO_2}.

Vascular

The final group of abnormalities of the heart and lung associated with dyspnea is pulmonary vascular disease (Chap. 8). When pulmonary hypertension is present because of diffuse obstruction of the pulmonary vascular bed, either by emboli or by changes in the lung blood vessels, dyspnea may result. This is considered to be largely the result of reflex hyperventilation. It may not be accompanied by alteration of ventilatory function, and insufficient data are at hand to know whether or not there is an accompanying reduction of the

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cardiopulmonary function in the various types of disorders that cause dyspnea are summarized in Table 5

REFERENCES

ARD R V and TWINING R H Evaluation of Valsalva test in bedside diagnosis of dyspnea. *Am J M Sc 234* 403 1957

BROWN C C. JR FRY D L. and EBERT R. V Mechanics of pulmonary ventilation in patients with heart disease *Am J Med 17* 438 1954

CHRISTIE R. V Dyspnea a review *Quart J Med 7* 421 1938

COMROE J H JR Dyspnea. *Mod Concepts Cardiovas Dis* 25 347 1956

MARSHALL R STONE R W and CHRISTIE R V The relationship of dyspnea to respiratory effort in normal subjects mitral stenosis and emphysema *Clin Sc 13* 625 1954

McILROY M B Dyspnea and the work of breathing in diseases of the heart *Prog Cardiovas Dis 1* 284 1959

SAXTON G A JR RABINOWITZ, M DEXTER, L. and HAYNES F The relationship of pulmonary compliance to pulmonary vascular pressures in patients with heart disease *J Clin Invest 35* 611 1956

diffusing capacity although such is likely if the pulmonary capillary bed and hence the size of the surface available for gas exchange are reduced Arterial blood gas analysis reveals reduced P_{CO_2}, because of the hyperventilation *The arterial oxygen saturation is usually normal* or slightly reduced Pulmonary hypertension is always present in these patients and the diagnosis of pulmonary vascular disease may be established or excluded by measurement of the pulmonary vascular resistance by cardiac catheterization

TABLE 5

Disease	*Cause of dyspnea*	*Physiological abnormality*
Heart failure	Congested stiff lungs Reflex tachypnea	Elevated pulmonary capillary pressure *Reduced lung compliance* Reduced vital capacity Reduced arterial P_{CO_2} Subnormal cardiac output Abnormal Valsalva
Pulmonary fibrosis	Stiff lungs Reflex tachypnea	Reduced diffusing capacity Reduced lung compliance Reduced vital capacity Reduced arterial P_{CO_2} Hypoxemia (in severe cases) aggravated by exercise relieved by O_2
Obstructive pulmonary disease	Resistance to air flow in and out of lungs	CO_2 retention and hypoxemia if severe Expiratory delay on spirography
Pulmonary vascular disease	*Reflex tachypnea*	*Normal ventilatory function* Reduced arterial P_{CO_2} Reduced diffusing capacity? Pulmonary hypertension

SUMMARY

In summary, dyspnea occurs most commonly when the work of breathing becomes excessive This happens when each breath is made difficult by stiff lungs or by airway obstruction or when the respiratory rate is unduly rapid It occurs in normal people during heavy activity which requires a large amount of respiratory effort and during mild activity in patients with cardiopulmonary disease *The reasons* for increased respiratory work and the accompanying alterations of

During exercise the tissues produce increased amounts or carbon dioxide and consume increased amounts of oxygen There is a corresponding increase of the output of carbon dioxide into the alveoli and of the consumption of oxygen from the alveoli If alveolar ventilation did not change the alveolar carbon dioxide concentration would rise and the alveolar oxygen concentration would fall Actually the alveolar ventilation does increase because of increase in the rate and in the depth of total ventilation As a result there is little alteration of the alveolar gas composition The cause of this hyperpnea is not entirely clear but it apparently results from stimulation of the respiratory centers by multiple factors The net result is relative constancy of alveolar and arterial blood gas tensions

Increased Diffusion

The other demand on pulmonary function is the diffusion of increased amounts of oxygen across the alveolar-capillary membrane This is achieved by three mechanisms (1) development of an increased pressure gradient for diffusion of oxygen across the alveolar membrane (2) increased rate of blood flow through the alveolar capillaries and (3) increase of the "diffusing capacity of the lungs

INCREASED PRESSURE GRADIENT FOR DIFFUSION The rate of diffusion of oxygen from the alveoli into the alveolar capillary blood is dependent upon the diffusing capacity of the lung and upon the pressure gradient of oxygen the difference between the partial pressure of oxygen in the alveoli and in the blood (Chap 1) During exercise the alveolar oxygen tension tends to stay constant in the normal subject However the oxygen tension in the venous blood falls (see below Increased Tissue Extraction of Oxygen) As a result the pressure gradient of oxygen between the alveolar air and the blood entering the alveoli is increased This causes an increase in the rate at which oxygen diffuses across the alveolar membrane

INCREASED RATE OF BLOOD FLOW THROUGH ALVEOLAR CAPILLARIES A more important mechanism for increasing the rate of diffusion across the alveolar-capillary membrane is provided by the increased rate of blood flow through the alveolar capillaries a result of the increased cardiac output (see below) Since more venous

CHAPTER 13

MUSCULAR EXERCISE

Muscular exercise represents a physiological stress to which all people are subject to some degree It is of interest to examine the normal mechanisms of adaptation to exercise, the requirements made of the cardiorespiratory system how these adaptations may fail in disease, and the methods available for detecting such failure Evaluation of the work tolerance of patients with cardiopulmonary disease should be based on an understanding of the physiological response to exercise

PHYSIOLOGICAL REQUIREMENTS IN EXERCISE

Muscular exercise places a demand on the cardiorespiratory system to supply increased amounts of blood to the exercising muscles The magnitude of this requirement depends upon the amount of work performed Ample data are at hand as to the amount of oxygen required for various types of activity For example Passmore and Durnin have indicated that sitting driving a car, or playing a musical instrument doubles the resting oxygen consumption and that slow bicycling or dancing triples it If data are not available the energy required for a task may be readily estimated by measuring an individ ual s oxygen consumption while he performs that task

PULMONARY ADAPTATIONS

Increased Alveolar Ventilation

How is this demand for more oxygen met by the cardiorespiratory system? In the case of the lungs it is met by increased alveolar venti lation and by increased diffusion of oxygen across the alveolar mem brane so that there is no alteration of the arterial blood gas composition

output is also responsible for the increased rate of blood flow through the alveolar capillaries as mentioned above

Increased Heart Rate

An increase of cardiac output may result either from an increase of heart rate or from an increase of stroke volume An increase of heart rate is the more important factor in the increase of cardiac output that occurs during exercise

The mechanism for the increase of heart rate during exercise is not entirely clear Increase of body temperature and the internal secretion of adrenalin may be factors Two causes of reflex tachycardia are reduction of tissue oxygen tension and reduction of blood pressure secondary to dilatation of arterioles in the exercising limbs In both cases tachycardia serves to maintain homeostasis Increased heart rate leads to increased cardiac output which tends to elevate the tissue oxygen tension it also causes increased blood pressure (Chap 1)

Increased Stroke Volume

An increase of stroke volume may also contribute to the increased cardiac output Stroke volume increases if the ventricle contracts more forcefully and expels more blood with each heart beat At rest the normal ventricle only expels one half of its diastolic volume and thus considerable reserve is available for ejection An increase of stroke volume might also result from increased end diastolic volume as a result of increased venous return from the exercising muscles As pointed out in Chapter 1 the force of ventricular contraction depends upon the degree to which the myocardial fibers are stretched at the end of diastole the end diastolic volume Increased end diastolic volume would lead to a more forceful ventricular contraction and hence increased stroke volume

Recent studies have indicated that the end diastolic size of the ventricle is normal or even reduced during muscular exercise The ventricle contracts with increased force even though it is not stretched more during diastole than it is at rest During muscular exercise presumably because of neurohumoral stimulation ventricular function changes (Chap 4) The heart operates on a higher ventricular function curve For a given degree of stretch it generates more stroke work during exercise than at rest and stroke volume is increased

blood enters the alveolar capillaries during each minute more oxygen diffuses out of the alveoli into the blood in each minute One might expect that the blood would flow through the alveolar capillaries so rapidly that there would be insufficient time for enough oxygen to diffuse into the blood to bring the oxygen saturation up to normal However, the normal diffusing capacity for oxygen is so great that at rest the oxygen tension in the blood traversing the alveolar capillary approaches the oxygen tension in the alveolus long before the blood reaches the end of the capillary This means that the blood may flow through the alveolar capillaries much faster than it does at rest and still take up its full quota of oxygen Since each unit of blood takes up its normal quota of oxygen and since much more blood flows through the alveoli in a given interval of time the amount of oxygen diffusing across the alveolar membrane in that interval of time is increased in direct proportion to the increased rate of blood flow

Increased Diffusing Capacity Finally, *there is actually* some increase of the diffusing capacity during muscular exercise This appears to be the result of expansion of the alveolar capillary bed so that there is an increased surface area available for diffusion of oxygen This means that the rate of diffusion of oxygen across the alveolar capillary membrane proceeds at an accelerated rate As a result of this and of the increased pressure gradient for diffusion oxygen diffuses across the alveolar capillary membrane so fast that even during very heavy exercise the blood leaves the alveolar capillaries with an oxygen tension which is almost as high as the alveolar oxygen tension

CARDIAC ADAPTATIONS

The second major area of adjustment to exercise involves the heart The tissue requirements for extra oxygen may be made up either by the extraction of increased amounts of oxygen from the blood which is flowing through the tissues an increased arteriovenous difference or by an increased supply of oxygen laden blood to the tissues an increase of the cardiac output During mild exercise, the increased oxygen uptake is about equally divided between these two mechanisms During heavier exercise, the burden falls increasingly upon the heart as the tissues reach the limit of their ability to extract oxygen from the blood flowing through them Increased cardiac

gen tension to be maintained at a relatively normal level an important mechanism for preventing hypoxia of the cells at the end of the capillary (Chap 11)

Reduced Blood Flow to Nonexercising Tissues

Nonexercising tissues also extract more oxygen from the blood flowing through them even though their metabolic rate is not increased During exercise vasoconstriction causes diminution of the

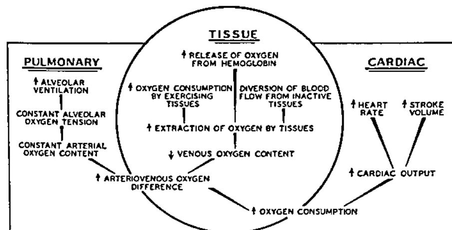


Fig 26 Schemat c s mmary of facto wh ch pro de ı c e sed o ygen con mpt on d r g musc la exerc e S nc al eolar nt la! o ı es n proport on to o yg pt ke al e olar o yge t o a d art r al o ygen co tent do ot fall Inc a d e I act on of o yg n f om blood flow g th o gh c g m scles the cha ge the o yhemoglob n d oc t o curve wh ch serves to release mo e o yg for a g en d op of Po and the d s on of blood to the m scles f om nact e t ssues all low r th venous oxygen cont t Th s c uses a inc eas d A V o yg d ff rence The ıncreas d o yg consumpt on is mad up by this I cr ed A V o yg d ff r nc and by the i crea d a d ac o tp t The latt ıs due both to c ea d heart rat and to ncreased stroke volum

blood flow to these tissues They continue to take up normal amounts of oxygen from the blood with the result that when the blood flow is reduced they must extract increased amounts of oxygen from each unit of blood This increased extraction of oxygen is aided by the change in the character of the oxygen dissociation curve mentioned above Reduction of the oxygen saturation of the blood leaving the inactive tissues contributes to the reduction of the oxygen saturation of the mixed venous blood and hence to the increased mean arteriovenous oxygen difference which is characteristic of muscular exercise

Together, the tachycardia and the change in ventricular function cause an increase in cardiac output which is adequate to meet the needs of the exercising organism These responses appear to be under the control of neuro regulatory centers which so regulate the cardiac output as to maintain homeostasis This is similar to the neural regulation of the magnitude of the alveolar ventilation, the rate and depth of respiration being so controlled as to maintain just enough alveolar ventilation to keep the alveolar gas composition constant in the face of a changing metabolic rate

INCREASED TISSUE EXTRACTION OF OXYGEN

The increased oxygen consumption that occurs during exercise is *not matched exactly by increased cardiac output This means that* the tissues must extract increased amounts of oxygen from the blood flowing through them When the cells consume increased amounts of oxygen the partial pressure of oxygen in and around the cells falls This causes an accelerated rate of diffusion of oxygen out of the capillary blood into the cells As a result, more oxygen is extracted from the blood flowing through the tissues and the venous oxygen saturation falls

In addition to the increased oxygen consumption of the exercising tissues there are two other important mechanisms which provide for *increased extraction* of oxygen from the blood There is a change in the character of the oxygen dissociation curve of hemoglobin so that more oxygen is yielded at a given partial pressure and there is a reduction of blood flow to nonexercising tissues so that these tissues also extract more oxygen from the blood flowing through them

Increased Release of Oxygen from Hemoglobin

As mentioned above a fall of oxygen tension in and around metabolically active cells leads to diffusion of increased amounts of oxygen out of the blood into the cells In addition the increased metabolic rate leads *to increased carbon dioxide tension and/or decreased* pH of the blood This causes a change in the character of the oxygen dissociation curve of hemoglobin less oxygen is combined with hemoglobin at a given partial pressure As a result increased amounts of oxygen are given up to the tissues without an increased fall of the partial pressure of oxygen in the blood This enables the venous oxy

sumption Finally, the venous pressure is usually apt to be elevated in heart failure This is particularly true during muscular exercise when the impaired heart cannot pump forward the increased venous return from the exercising limbs

Impaired cardiac function may be the result either of valvular disease or of impaired myocardial function The general abnormalities mentioned above decreased cardiac output excessive tachycardia and elevated venous pressure are apt to be present in cardiac limitation of any type In addition specific physiological abnormalities are associated with each type of heart disease and are discussed in Chapters 3 and 5

CLINICAL IMPLICATIONS OF EXERCISE STUDIES

WORK EVALUATION

By appropriate study one can learn what level of exercise a patient can tolerate with comfort and what factors are responsible for limitation of his ability to do muscular exercise Observation of a patient during exercise particularly if carried out in conjunction with measurement of some of the parameters mentioned above is a useful supplement to a careful clinical history The latter probably represents the most useful measure available for work evaluation since a level of work which produces symptoms is in general excessive

Further experience may delineate measurements of exercise tolerance which will provide objective indexes that are more valid than a patient s symptoms For example it may be that in a patient with heart disease performance of a given task is associated with an inadequate cardiac output before symptoms occur If such can be shown to be detrimental to the patient measurement of cardiac output or possibly of pulse rate during exercise may become very useful in establishing a patient s safe level of work tolerance

It is difficult to translate this type of information into clinical practice Many forms of exertion are of the sudden spurt type They require the instantaneous expenditure of large amounts of energy which may be available through anaerobic metabolism This is manifest later as oxygen debt energy which is available for a brief period of time but which must be paid off later during a period of rest The degree to which a patient can incur an oxygen debt with

and which reflects the fact that increased amounts of oxygen are extracted from the blood by the whole body

The factors which provide the increased oxygen uptake during muscular exercise are outlined schematically in Figure 26

FAULTY PHYSIOLOGICAL ADAPTATIONS TO EXERCISE

INADEQUATE PULMONARY FUNCTION

In what types of disease are these adjustments imperfect and how may this be manifest? The alterations of arterial blood gas composition characteristic of inadequate ventilation and of impaired diffusion have been discussed in Chapter 11 When work tolerance is limited by impaired ventilatory function reduction of the vital capacity and/or expiratory delay are generally evident on spirography (Chap 6) In addition arterial hypoxemia and carbon dioxide retention are present particularly so in diseases involving obstruction to the flow of air in and out of the lungs, such as pulmonary emphysema (Chap 6), but they may also occur in pulmonary fibrosis or in the aveolar hypoventilation syndrome (Chap 7)

In patients with a diffusion limitation usually due to pulmonary fibrosis (Chap 7) exercise is characterized by a precipitous fall of the arterial oxygen saturation without rise of the arterial carbon dioxide tension (Chap 11) The work tolerance of such patients may be assessed by measuring the arterial oxygen saturation at different levels of exercise in order to determine at what level of work diffusion becomes inadequate so that hypoxemia appears Also, by measuring the diffusing capacity of the lung, one can predict the level of oxygen consumption that the patient is able to sustain

INADEQUATE CARDIAC FUNCTION

What measurements characterize the patient whose cardiac output is inadequate for a given task? The cardiac output may be measured directly and compared to the normal value for that level of oxygen consumption If it is low it is probably inadequate A clue to the presence of inadequate cardiac output is excessive tachycardia during exercise In patients with heart failure the stroke volume may actually fall during exercise (Chap 4) and thus the heart rate may increase excessively and be abnormally rapid for each level of oxygen con

heart so called 'athletes heart The latter is relatively larger and stronger than normal It beats more slowly and more forcefully than the normal and presumably is capable of greater work Again this is only of direct advantage to the individual in enabling him to do harder and more sustained work There is no evidence that the myocardial blood supply is increased out of proportion to the increased myocardial muscle mass and the athlete s heart may be no better able than the normal to withstand the effects of occlusive coronary artery disease

It would appear then that exercise causes physiological changes which enable the individual to do more work but there is no evidence that such changes are of value in terms of general health or of ability to withstand the effects of cardiopulmonary disease Exercise is apparently capable of reversing the physiological abnormalities encountered in neurocirculatory asthenia (Chap 5) and it may have desirable effects as an adjunct to the control of obesity and on the state of mind the bowel habits and the stature Otherwise until more information is available there would appear to be no compelling reason for a sedentarily inclined individual to indulge in muscular exercise

REFERENCES

ASMUSSEN E and NEILSEN M Cardiac output during muscular work and its regulation *Physiol Rev 35* 778 1955

ASTRAND P O Human physical fitness with special reference to sex and age *Physiol Rev 36* 307 1956

BARRATT BOYES B G and WOOD E H Hemodynamic response of healthy subjects to exercise in the supine position while breathing oxygen *J Appl Physiol 11* 129 1957

BECKNER G L and WINSOR T Cardiovascular adaptations to prolonged physical effort *Circulation 9* 835 1954

DILL D B HORVATH S M and CRAIG F N Responses to exercise as related to age *J Appl Physiol 12* 195 1958

DONALD K W BISHOP J M CUMMINGS G and WADE O L The effect of exercise on the cardiac output and circulatory dynamics of normal subjects *Clin Sc 14* 37 1955

GREGG D E SABISTON D C and THEILEN E O Performance of the heart changes in left ventricular end-diastolic pressure and stroke work during infusion and following exercise *Physiol Rev 35* 130 1955

HICKAM J B and CARGILL W H Effect of exercise on cardiac output and pulmonary arterial pressure in normal persons and in patients with cardiovascular disease and pulmonary emphysema *J Clin Invest 27* 10 1948

out harm is not known Oxygen debt can be calculated by measuring oxygen consumption before, during and after performance of a task An abnormally large oxygen debt suggests cardiac impairment and probably should be avoided Abnormal oxygen debt also correlates well with abnormal tachycardia, particularly during the recovery period Patients who develop abnormal oxygen debt during exercise also reveal abnormally slow return of pulse rate to normal *The degree to which these measurements of work tolerance are* superior to clinical evaluation remains to be proved and it is particularly important to discover what degree of abnormality of these parameters represents evidence that the associated task is detrimental to the patient

BENEFICIAL EFFECTS OF EXERCISE

A recurrent question has been What degree of exercise is harmful to a patient? Just as difficult a problem is 'What degree of exercise is of benefit? Exercise which causes hypoxia is presumed to be harmful On the other hand a moderate degree of hypoxia may actually be *beneficial by causing growth of collateral blood vessels to the part* suffering from oxygen lack

Aside from this highly theoretical possibility are there objective benefits to be derived from muscular exercise? As an aid to correction or prevention of obesity, it is obviously good Many people also obtain psychological benefit from exercise But are there direct physiological benefits? To attempt to answer this, one must examine the chronic effects of muscular exercise on the organism Any muscle that is subjected to increased work loads becomes hypertrophied This is true of the limb muscles of the muscles of respiration and of the heart In the case of the former the only known physiological advantage is the ability to do more and harder work There are no known direct effects on the health of the individual as a whole Increased strength of the respiratory muscles is also of dubious value Even if the trained athlete has a greater than normal maximal breathing capacity he is no better able to withstand the consequences of pulmonary disease such as fibrosis or emphysema Limitation of respiratory function is rarely related to the power of the thoracic muscles so that increase of their strength is of no particular advantage

Controversy has long raged about the effects of exercise on the

CHAPTER 14

TESTS OF CARDIOPULMONARY FUNCTION IN CLINICAL MEDICINE

A primary intention of this book has been to present an explanation of cardiopulmonary physiology in health and disease as a basis for understanding and interpreting the various tests of cardiopulmonary function that are available From the preceding chapters the indications for these tests should be fairly obvious and the meaning of the results that one may obtain should be clear This chapter is a recapitulation of some of that material in order to summarize when and how the specific tests are of value to the physician in the diagnosis and treatment of his patients

RIGHT HEART CATHETERIZATION

Technique

Right heart catheterization is generally performed by insertion of a catheter into an antecubital saphenous or femoral vein under local anesthesia The catheter which is radiopaque is then advanced into the right atrium right ventricle and pulmonary artery under fluoroscopic control Information is provided (1) by visualization of the position of the catheter when and if it enters the left side of the heart aorta or pulmonary veins through abnormal channels (2) by measurement of the oxygen content of the blood in the various chambers of the heart (3) by injection of dye or of other indicator substances into the various chambers of the heart and sampling their concentration in the blood stream in another location and (4) by measurement of the pressure in the various chambers of the heart (Chap 2) Although arrhythmias are often seen as the catheter is passed through the various chambers of the heart the procedure is generally without

MITCHELL J H SPROULE B J and CHAPMAN C B The physiological meaning of the maximal oxygen intake test *J Clin Invest* *37* 538 1958
PASSMORE R and DURNIN J V G A Human energy expenditures *Physiol Rev* *35* 801 1955
SANCETTA S M and RAKITA L Response of pulmonary artery pressure and total pulmonary resistance of untrained convalescent man to prolonged mild steady state exercise *J Clin Invest* *36* 1138 1957
THEILEN, E O GREGG D E and ROTTA A Exercise and cardiac work response at high altitude *Circulation* *12* 383 1955

patients with characteristic physical and roentgen signs do not require catheterization indeed most patients with patent ductus arteriosus do not require this test for accurate diagnosis In doubtful cases the investigation should be carried out and this applies to patients suspected of having functional murmurs in whom definitive diagnosis is mandatory

The functional consequences of many congenital lesions require this type of physiological evaluation in order to make a decision for or against surgery The level of the pulmonary artery pressure is often of great importance in deciding that surgery is indicated or that it would be too hazardous In pulmonary stenosis for example a markedly elevated systolic pressure in the right ventricle is an indication for pulmonic valvulotomy (Chap 3) In septal defects or patent ductus arteriosus on the other hand a systolic pressure in the right ventricle which is similar to or higher than that in the aorta is a contraindication to surgery

Right heart catheterization is also useful in evaluating certain types of acquired heart disease Characteristic pressure tracings may be helpful in making a diagnosis of constrictive pericarditis (Chap 5) The level of pulmonary artery pressure particularly in conjunction with measurement of the cardiac output at rest and during exercise is helpful in defining the stage and the severity of mitral stenosis (Chap 5) The level of the end-diastolic pressure in the right ventricle is an indication of the presence or absence of right ventricular failure (Chap 4) Finally as mentioned below the use of cardiac catheterization to measure the cardiac output has many applications in the evaluation of patients with cardiopulmonary disease

Limitations

There are many ways in which the results of right heart catheterization may be interpreted erroneously particularly with respect to the diagnosis of congenital lesions As discussed in Chapter 2 a large left to right shunt may be associated with a measurable pressure gradient across the pulmonic valve leading to an incorrect diagnosis of pulmonic stenosis Left to right shunts involving 25 per cent of the flow into the involved chamber of the heart may escape detection by the oxygen step up" technique because the amount of flow is too small to alter the oxygen saturation of the venous blood For this reason a clinical diagnosis of ventricular septal defect need not be

TABLE 6 NORMAL VALUES FOR SOME PARAMETERS OF CARDIOPULMONARY FUNCTION

PRESSURES IN THE CARDIOVASCULAR SYSTEM	
Pulmonary artery	25/8 mm Hg
Right ventricle	25/0 mm Hg
Right atrium	3 mm Hg
Systemic veins	100 cm H_2O
Systemic arteries	120/80 mm Hg
Left ventricle	120/4 mm Hg
Left atrium	5 mm Hg
Pulmonary capillary (wedge)	5 mm Hg
BLOOD FLOW	
Resting cardiac index	3 0 liters/min /sq meter B S A
LUNG MECHANICS	
Lung compliance	0 2 liter/cm H_2O
Airway resistance	1 6 cm H O/liter/sec
VENTILATORY FUNCTION AND LUNG VOLUMES	
Maximal mid expiratory flow	4 0 liters/sec
Vital capacity	5 0 liters
Timed vital capacity	98% in 3 seconds
Maximum breathing capacity	150 liters/min
Residual vol /total lung capacity	27%
7 nitrogen	<2%
DIFFUSING CAPACITY	
Rest	15 cc CO/min /mm Hg
Exercise	25 cc CO/min /mm Hg
ARTERIAL BLOOD GASES	
Oxygen saturation	97%
Oxygen content	20 volumes %
Oxygen tension	96 mm Hg
Carbon dioxide tension	40 mm Hg
pH	7 40

risk except in seriously ill patients particularly those with cyanosis due to congenital heart diseases or those with disorders such as primary pulmonary hypertension or Ebstein s anomaly of the tricuspid valve (Chap 3)

Indications

This procedure is indicated for the definitive diagnosis of valvular lesions of the right side of the heart and intracardiac shunts Many

secondary to aortic stenosis from that due to ischemic heart disease A systolic pressure gradient between the left ventricle and aorta indicates the presence of hemodynamically significant aortic stenosis The absence of a gradient suggests that although stenosis may be present and may cause the characteristic murmur and thrill it is not of hemodynamic significance and that ischemic heart disease is mainly responsible for the patient s symptoms Thus although this procedure is generally not necessary in order to make a diagnosis of aortic stenosis it should be done before surgery in order to make sure that the lesion is of consequence to the patient

Limitations

The number of patients who have been subjected to this technique is far smaller than that of patients who have undergone right heart catheterization and its risk is difficult to assess At the present time its use is generally limited to those patients in whom the information to be derived will be decisive in deciding for or against surgery of the mitral or aortic valve

CARDIAC OUTPUT

Technique

Cardiac output may be measured by the Fick principle (Chap 1) This requires simultaneous collection of samples of (1) mixed venous blood obtained from the right ventricle or pulmonary artery (2) arterial blood and (3) expired air Mixed venous blood is difficult to obtain but may be collected during right heart catheterization (see above) In many individuals a polyethylene catheter can be inserted into the right ventricle or pulmonary artery for this purpose

Cardiac output may also be measured by dye or isotope dilution techniques These require injection of the indicator material into a peripheral vein whereupon arterial blood is collected through a suitable detecting instrument This type of technique is without significant risk and imposes very little discomfort on the patient

Indications

In some cases of congestive heart failure of unknown etiology the level of the cardiac output may be helpful in arriving at the correct diagnosis A high cardiac output suggests thyrotoxicosis anemia em

deemed incorrect if catheterization findings are normal Valvular insufficiency may lead to the finding of an oxygen step up in the chamber of the heart proximal to that involved in a left to right shunt, and so a ventricular defect may be misdiagnosed as an atrial septal defect On the other hand poor mixing of shunted blood may make it appear as if the shunt were one chamber distal to that actually involved, so that an atrial defect may be incorrectly called a ventricular septal defect Analysis of many samples of blood will generally obviate most of these errors, and the introduction of dye and other techniques has greatly increased the accuracy and the sensitivity of the technique

Right heart catheterization is not helpful in revealing the presence or absence of lesions in the left heart, but the secondary effects of such lesions on the pulmonary circulation may be assessed Although the risk is slight in most patients the discomfort the need for radiation, and the occasional but not serious aftermath of phlebitis require that definitive indication be present before the procedure is employed Its use is restricted to laboratories in which the procedure can be carried out by experienced, trained personnel

LEFT HEART CATHETERIZATION

Technique

This procedure may be performed by inserting a needle into the left atrium through the back through a bronchoscope, through the superior mediastinum or through the atrial septum A catheter may then be threaded through the needle into the left ventricle An alternative technique is to insert a needle directly into the left ventricle through the anterior chest wall Information is derived from pressure measurements dye dilution curves and measurement of the oxygen saturation of the blood in the left atrium and left ventricle

Indications

This technique is indicated primarily for the evaluation of mitral stenosis and aortic stenosis In the case of the former, left heart catheterization may be necessary to establish the presence of hemodynamically significant mitral block and is valuable in distinguishing between mitral stenosis and mitral insufficiency (Chap 5) In aortic stenosis the diagnosis can usually be made clinically but it may be difficult to distinguish left ventricular failure or angina pectoris

As used clinically the measurement depends upon the subjective determination of the time of arrival of the indicator substance by the patient This may be very unreliable For this reason objective measurement with dye or with a breath holding technique is to be preferred The measurement of the circulation time is useful in following the course of a patient with congestive heart failure, but definitive assessment of hemodynamic events requires more elaborate study It is of great value clinically in that a short circulation time suggests the presence of the hyperkinetic state, a finding which may lead to the diagnosis of a specifically remediable lesion

ANGIOCARDIOGRAPHY

Technique

Roentgenographic outline of the cardiac chambers and great vessels is provided by the rapid injection of a contrast material into a basilic vein or through a catheter into the right side of the heart followed by a series of rapid exposures of x ray films Information is obtained by direct visualization of abnormal circulatory pathways if the shunt is from right to left by visualization of narrowed valves by visualization of the interior of the ventricles during systole and diastole in order to estimate heart size and the amplitude of ventricular contraction and by visualizing regurgitation through an insufficient valve Contrast material may also be injected into the left heart for visualization of the aortic and mitral valves and for detection of left to right shunts

Indications

This technique often provides the best definition of the site and extent of congenital lesions of the heart It is indicated in the preoperative evaluation of all cases of congenital heart disease in which catheterization studies do not reveal the diagnosis Studies are under way to apply this technique to the study of the pulmonary circulation and it is possible that angiocardiographic study of the blood vessels of the lung will provide useful information about the type and extent of pulmonary vascular disease particularly as a complication of heart disease

physema arteriovenous fistula or beriberi whereas most diseases leading to heart failure are associated with a low cardiac output The presence or absence of heart failure may be ascertained by measurement of the change of cardiac output after exercise and digitalization (Chap 4) Finally, dye or isotope dilution curves may be used to exclude many types of heart disease without resorting to cardiac catheterization a normal curve tending to exclude significant degrees of intracardiac shunt or valvular insufficiency (Chap 2)

Limitations

Although without risk and productive of very little discomfort to the patient measurement of the cardiac output is not often necessary *It is most useful to the clinical physiologist for study of the patho* physiology of cardiopulmonary disease

CIRCULATION TIME

Technique

The circulation time between two parts of the cardiovascular system may be measured by injection of an indicator substance into one portion of the circulation and detection of its time of arrival at another area Arm to lung circulation time is measured by timing the appearance of ether in the lung after its injection into a peripheral vein lung to ear circulation time is measured by oximetric recording of the time of onset of the rise of arterial oxygen saturation after breath holding or after an inspiration of oxygen arm to ear circulation time is measured by recording with an oximeter the appearance at the ear of dye injected into a vein a similar value is provided by the decholin and fluorescein techniques which are used clinically

Indications and Limitations

The circulation time depends upon the velocity of blood flow from the point of injection to the point of detection of the indicator substance and upon the dimensions of the circulatory pathway involved As such it is a reflection both of the cardiac output and of the size of the vascular bed between the points of injection and detection A high cardiac output is generally associated with a short circulation time and a low cardiac output particularly since it is generally associated with venous congestion causes a prolonged circulation time

falls during the last few seconds of the forced expiration (strain) After release of the strain the blood pressure rises above normal for a few seconds The fall of blood pressure is thought to result from decreased left ventricular output consequent to the period of diminished venous return to the right ventricle when the intrathoracic pressure was raised In heart disease the blood pressure remains elevated presumably because of the increased reservoir of blood in the heart and lungs and there is no overshoot after the strain is terminated The degree to which this test is useful in clinical medicine remains to be assessed

Limitations

The relative innocuousness of the technique has been mentioned and complications are rare if firm pressure is maintained over the site of arterial puncture for at least 10 minutes after withdrawal of the needle On the other hand the information to be derived from the measurement is of limited clinical value and measurement of the blood pressure by the sphygmomanometric technique is usually adequate

VENOUS PRESSURE

Technique

Insertion of a needle into a peripheral vein for measurement of the mean intraluminal pressure is a common clinical technique but one fraught with difficulties In assessing venous pressure one must estimate the height of the zero point of reference in relationship to the level of the heart in order to correct for the hydrostatic effect and one must make certain that the needle is patent inserted well into the vein and not against the wall

Indications

When properly performed estimation of the mean systemic venous pressure is a helpful guide to the presence or absence of congestive heart failure and to the response to therapy Recording of the central venous pressure by threading a polyethylene catheter through the needle may provide useful information in evaluating pericarditis and tricuspid insufficiency (Chap 5)

Limitations

There is a risk and a significant but low mortality with this procedure Contrast material may stream into one vessel, resulting in pulmonary or systemic embolism Cerebral embolism is particularly to be feared and embolism of a spinal artery has followed aortic angiography These risks can be minimized by proper control of the dose and concentration of the radiopaque material As in left heart catheterization the use of the technique should be limited to patients in whom it is necessary as part of the preoperative work up

ARTERIAL PRESSURE

Technique

Systemic pressure is easily measured by inserting a needle into a major artery and recording the intraluminal pressure fluctuations with a pressure transducer The arterial puncture is painless, but some discomfort may be present after the local anesthesia wears off The risk is negligible although the procedure should probably not be performed on patients with peripheral vascular disease The radial artery is a convenient site for puncture particularly if the needle is to be left in place during muscular exercise A brachial or femoral artery may also be used

Indications

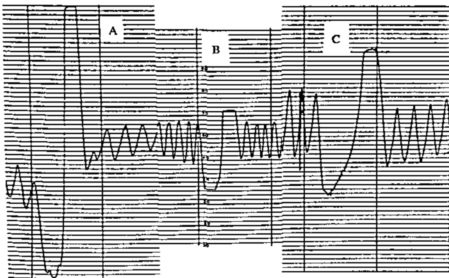
Arterial pressure tracings are necessary for accurate measurement of mean arterial pressure for calculation in conjunction with measurement of cardiac output of peripheral vascular resistance In obesity, a falsely high blood pressure may be recorded by the sphygmomanometric technique and determination of the intra arterial pressure may be necessary to decide whether or not hypertension is present Finally in aortic stenosis the rise of pressure to the systolic peak is characteristically delayed, and an arterial tracing may be helpful in arriving at a proper diagnosis

A special application of arterial pressure measurements has been suggested for the evaluation of dyspnea and is based upon measurement of the arterial pressure during and after a 10 second Valsalva maneuver Arterial pressure may be measured directly or by means of the sphygmomanometer Normally the onset of the Valsalva maneuver is followed by an abrupt rise of blood pressure which then

puts spirometry within reach of the doctor s office and the hospital ward or clinic

Indications

Spirometry is the first step in the physiological evaluation of the dyspneic patient The majority of patients with shortness of breath due to pulmonary disease have an abnormal spirogram The test is particularly indicated for the diagnosis and evaluation of pulmonary fibrosis bronchial asthma and pulmonary emphysema Patients with



F g 27 Typ c l sp og ams f om a o m l subj t (A) a pat nt w th pulmo ry fib o (B) and a p tient w th p lmo ary emphysem (C)

extensive pulmonary fibrosis reveal reduction of the vital capacity The extent of the fibrosis is reflected in the degree of reduction of the vital capacity and the improvement of the vital capacity serves as a guide to the efficacy of therapy as with steroids Patients with asthma and emphysema have decreased rates of airflow from the lungs during a forced expiration This may be evaluated by measurement of the maximal mid expiratory flow rate (M M F) or of the timed vital capacity Severe pulmonary emphysema is associated with an M M F consistently below 1 0 liter per second even after administration of bronchodilators (Chap 6) In asthma the M M F varies from day to day and when reduced is greatly improved by the administration

Limitations

Although the procedure is harmless it must be performed with care if it is to provide accurate information Interpretation of the results of the measurement must be based upon an understanding of the many factors that affect the height of the venous pressure (Chap 1)

MAXIMUM BREATHING CAPACITY

Technique

The maximum breathing capacity (M B C) is best determined by having the patient breathe as much air as possible into a bag in 15 seconds The volume of the air in the bag is measured and multiplied by four to determine the maximum breathing capacity expressed in liters per minute

Indications and Limitations

This test is primarily of value in screening patients suspected of having some form of pulmonary disease If the test is normal ventilatory function is probably normal On the other hand if the test is abnormal a variety of factors might be responsible These include poor effort on the part of the patient deformity of the bones joints or muscles of respiration obstruction to the flow of air through the airways or increased stiffness of the lungs Thus a normal M B C may be helpful information whereas a reduced value is of limited diagnostic aid

SPIROMETRY

Technique

Spirometric study provides a graphic record of the volume of air that can be expelled from the lung after a maximum inspiration (vital capacity) and of the rate at which that air can be expired It may also be used to record the rate and depth of ventilation The record is obtained by having the patient breathe in and out of a spirometer the movements of which are translated by means of a pen to a moving kymograph drum The technique is painless easy to perform and quickly carried out The recent availability of inexpensive equipment*

* Vitalor manufactured by McKesson Appliance Co Toledo Ohio

Indications

In patients with bilateral disease particularly tuberculosis bronchospirometry provides information of value in deciding how much if any surgery may be performed on each lung This type of study is also useful in patients with unilateral pleural disease in order to document restriction of lung function and hence the need for decortication

Limitations

As discussed in Chapter 9 the limiting factors in resectional lung surgery are not necessarily assessed by measurement of oxygen consumption and ventilation In many cases evaluation of the size of the pulmonary vascular bed is more important than is bronchospirometric study On the other hand bronchospirometry may be helpful in some patients For example absence of oxygen uptake on one side indicates that the lung may be removed without hazard whereas evenly divided function in a patient with over all impairment of pulmonary function suggests that resectional surgery should be limited Thoracoplasty may be the procedure of choice in such a patient

There are many pitfalls in the performance of bronchospirometry which may lead to inaccurate records and to erroneous interpretations The lungs must be properly separated by the bronchospirometric catheter so that the ventilation of each is measured separately At the same time a major bronchus should not be occluded by inserting the catheter too far into the lung Secretions must be aspirated so that the airways or catheter do not become occluded Finally since ventilation is carried out through the relatively narrow lumina of the bronchospirometric catheter the sum of the vital capacity of the lungs is generally less than that measured for the lung as whole However the degree to which each lung is contributing to the total vital capacity may be measured

MECHANICS OF BREATHING

Technique

Lung compliance and airway resistance may be calculated from measurements of intrapleural pressure and of the volume and rate of air flow into and out of the lung Intrapleural pressure is reflected in the esophageal pressure which may be measured by having a patient

of bronchodilators Spirometric evaluation is helpful in deciding which form of therapy is most effective in an individual patient

The vital capacity is a useful measure of pulmonary congestion The degree to which air containing alveoli are replaced by fluid or by dilated capillaries is reflected in the degree of reduction of the vital capacity Measurement of the vital capacity before and after therapy is helpful in assessing the effect of treatment

Spirometric studies are of some use in evaluating patients for thoracic surgery Severe restrictive or obstructive insufficiency is one contraindication to surgery (Chap 9)

Finally measurement of the ventilation is useful in administering artificial respiration either during anesthesia or to a respirator patient After estimation of total ventilatory requirements, pressures can be applied to produce the desired tidal volume as registered on the spirometer (Chap 10)

Limitations

Spirometric studies provide information about only one aspect of pulmonary function—external ventilation They should not be considered as definitive pulmonary function tests but must be interpreted in the light of the type of information that they are designed to reveal They are very widely employed and are simple to perform but are by no means the final word in the study of pulmonary function

BRONCHOSPIROMETRY

Technique

Designed to measure the oxygen uptake and ventilation of each lung this technique requires the insertion of a double lumen catheter into one major bronchus usually the left A balloon near the tip is inflated so that all the air from one lung passes in and out of one lumen of the catheter The remaining ventilation is carried out through the other lumen the orifice of which is in the trachea Another balloon proximal to this orifice prevents leakage The procedure is performed under topical anesthesia Ventilation from each lung is recorded on separate oxygen filled spirometers containing a CO absorber such as soda lime The record permits calculation of the oxygen consumption of each lung

developed in Chapter 1 the lung volume is of no functional consequence except to prevent variation of alveolar gas composition during the respiratory cycle In pulmonary fibrosis the total lung capacity is reduced with symmetrical reduction of the various components, so that the ratio of residual volume to total lung capacity is normal (30 per cent or less) In emphysema the total lung capacity is normal or increased but the outstanding abnormality is inability to empty the lungs normally so that the residual volume and functional residual capacity are greatly increased In addition uneven distribution of inspired air to the various parts of the lung is reflected in an abnormal dilution curve of a foreign gas After breathing oxygen for 7 minutes the alveolar nitrogen concentration is greatly in excess of the normal 2 per cent because of the delayed washout of nitrogen from poorly ventilated areas of lung These guides provide indexes to the severity of emphysema but the deleterious functional consequences of this disease are related to airway obstruction pulmonary vascular changes and to abnormality of arterial blood gas composition Although these tests provide interesting information they require expensive equipment and are not necessary for adequate evaluation of most patients with cardiopulmonary disease

ARTERIAL BLOOD GASES

Technique

The technique of arterial puncture has been mentioned above (Arterial Pressure) Blood gas analysis is most accurately performed by the Van Slyke manometric technique which measures the amount of oxygen and carbon dioxide in the blood The oxygen saturation of the blood is calculated by dividing the oxygen content by the oxygen capacity after subtracting the amount of oxygen dissolved in the plasma in each sample The oxygen capacity is obtained by measuring the amount of oxygen in the blood after the hemoglobin has been completely saturated by exposure to air for 30 minutes This type of analysis requires a trained technician and equipment which costs approximately $500 Duplicate analyses can be carried out in 30 minutes An alternative method for measurement of blood oxygen saturation is the spectrophotometric technique which is sufficiently accurate and relatively easier to learn but which requires equipment which is about four times as expensive Furthermore this technique

swallow a small plastic tube Air movement into and out of the lung may be recorded on a rapidly moving spirometer or on a pneumo tachygraph The latter measures velocity of airflow and integration of the record provides measurements of volume

Indications and Limitations

Lung compliance and airway resistance may be measured with little difficulty in most patients Unfortunately the calculated values for these parameters of respiratory mechanics may be inaccurate since the esophageal pressure may not be truly representative of the intra pleural pressure Since reduced lung compliance is usually associated with reduction of the vital capacity and since increased airway resist ance is generally accompanied by expiratory delay on spirometry, clinical estimation of ventilatory function with a spirometer is usually adequate, and the more refined measurements of ventilatory mechanics are not often necessary

LUNG VOLUME AND MIXING

Technique

Measurement of total lung volume and in conjunction with spi rometry of the subdivisions of lung volume, is carried out by having a patient breathe a foreign gas while expired air is collected for sub sequent analysis Either oxygen or helium may be used and a con tinuous record of the expiratory nitrogen or helium concentration provides an estimate of the efficiency with which gases are mixed in the lung Continuous analysis of the nitrogen content of a single forced expiration after a breath of oxygen also provides an index of lung mixing In normal subjects the oxygen is evenly distributed throughout the lung so that expiration consists of dead space gas which is the same as the inspired mixture followed by alveolar gas of constant composition Poor mixing of gases in the lung is indicated by expiration of alveolar gas of increasing nitrogen concentration as air is delivered from alveoli that were less and less ventilated by the single breath of oxygen

Indications and Limitations

Measurement of the subdivisions of the lung volume may be help ful in evaluating pulmonary fibrosis and emphysema although as

not usually associated with carbon dioxide retention Hypoxemia due to impaired diffusion is a grave prognostic sign

Two other situations which require arterial blood gas analysis for proper evaluation are polycythemia and cyanosis (Chap 11) Measurement of the arterial oxygen saturation is necessary in order to distinguish between primary and secondary polycythema Although mild hypoxemia may be present in polycythemia vera, an arterial oxygen saturation of less than 90 per cent suggests the presence of underlying cardiopulmonary disease Conversely if the arterial oxygen saturation is over 95 per cent primary polycythemia is probably present Since cyanosis is an unreliable index of hypoxemia adequate evaluation of the cyanotic patient requires arterial blood gas analysis

Limitations

Arterial blood gas analysis is useful in the evaluation of pulmonary insufficiency On the other hand moderate derangement of pulmonary function need not be associated with any abnormality of arterial blood gas composition In particular, a relatively large (20 per cent) right to left shunt must be present before hypoxemia is present and so exclusion of a small shunt requires a more sensitive technique such as a dye dilution curve (Chap 2) Also severe impairment of diffusion must be present before the arterial oxygen saturation falls As a result adequate evaluation of pulmonary fibrosis requires measurement of the diffusing capacity of the lung (Chap 7)

DIFFUSING CAPACITY

Technique

The diffusing capacity of the lung for oxygen may be measured directly or from measurement of the diffusing capacity for carbon monoxide The former requires an arterial puncture but the latter does not Both techniques are innocuous but require a good deal of technical analysis or special instrumentation They are both based upon the fact that the diffusing capacity is equal to the gas uptake divided by the difference between the partial pressure of the gas in the alveoli and that in the mean capillary blood Gas uptake is measured easily whereas alveolar gas tension is difficult to measure in individuals with poor mixing of gases in the lung and thus in

does not provide measurement of the CO_2 content of the blood The arterial P_{CO_2} can be measured directly by the 'bubble equilibration technique, which is relatively inexpensive, but which is extremely difficult from the technical standpoint A number of manufacturers are developing equipment for direct estimation of blood P_{CO} which promises to be relatively simple of operation but which will probably be extremely expensive At the present time arterial blood gas measurements are probably best performed by Van Slyke manometric analysis for O_2 and CO_2 content and by direct measurement of the pH The oxygen saturation and P_{CO_2} may then be calculated from these data Campbell and Howell have recently reported a rebreathing technique for measuring the arterial P_{CO_2} which promises to be of great clinical value since it can be performed at the bedside and does not require an arterial puncture

Indications

Like spirometry arterial blood gas analysis is essential for the proper evaluation of patients with pulmonary insufficiency The measurement should be available to the practicing physician and the cost of the laboratory analyses is not beyond the reach of most hospitals With a little training the physician can learn to collect an air free sample of arterial blood so that if laboratory facilities are available he can perform this test on his patients

Measurement of the arterial oxygen saturation and the P_{CO_2} is helpful in determining the type and severity of pulmonary insufficiency (Chap 11) This, in turn has diagnostic prognostic and therapeutic significance Ventilatory insufficiency is characterized by relatively more carbon dioxide retention than hypoxemia Precise regulation of artificial ventilation is dependent upon periodic measurement of the arterial P_{CO} Right to left shunts in the heart or lung are characterized by hypoxemia incompletely relieved by breathing oxygen The severity of the shunt is reflected in the degree of hypoxemia Relative impairment of distribution of blood and gas in the lungs as occurs in emphysema leads to elevation of the arterial P_{CO} and reduction of the arterial oxygen saturation The latter is relieved by oxygen breathing The severity of the process is reflected in the degree of abnormality of arterial blood gas composition Finally severe impairment of diffusion is characterized by hypoxemia which is exaggerated by exercise overcome by oxygen breathing and

on a treadmill at various rates and grades or pedalling a stationary bicycle Measurements include pulse rate, arterial blood gas composition, cardiac output pressures within the circulatory system and thorax oxygen uptake and diffusing capacity

Indications

Study of a patient during exercise may be necessary in order to demonstrate a cardiopulmonary abnormality not detectable at rest Only during periods of increased pulmonary blood flow may pulmonary hypertension be present in many forms of cardiopulmonary disease in mild disorders of cardiac function the cardiac output may be normal at rest but may fail to rise normally during exercise, hypoxemia due to a diffusion limitation may only be present during exertion

Measurement of the maximum work that a person can perform is a useful index of over all cardiopulmonary function In addition observation and study of the patient during the maximum work of which he is capable lends insight into the nature of his limitation Leg fatigue rather than dyspnea may turn out to be the limiting symptom Dyspnea may be associated with normal arterial blood gas composition in which case cardiac function rather than impaired pulmonary function is probably the limiting factor Finally the specific measurements discussed previously may help to pinpoint the nature and extent of the functional abnormality which limits the patient s ability to do work

Exercise tests may prove useful in work evaluation Knowledge of the amount of oxygen that is consumed during the performance of various jobs permits translation to industry of information derived in the laboratory If the patient s maximum oxygen uptake has been measured it becomes possible to decide what jobs are within his capabilities Further work is needed before objective measurements may be used as reliable guides for work and disability evaluation and it is likely that these guides will be different in various diseases For example the level of ventilation or intrapleural pressure swing may be the limiting factor for a patient with emphysema whereas cardiac output or possibly pulse rate may be the important guides to the amount of work that a patient with heart disease can perform with safety

homogeneous alveolar gas composition In such individuals a mean alveolar gas value is generally calculated from the arterial blood carbon dioxide tension

Indications

Pulmonary fibrosis in patients who have little or no reduction of vital capacity may be assessed by measurement of the diffusing capacity (Chap 7) This measurement provides diagnostic information, and although a clue to the diagnosis may be present in the spirographic finding of hyperventilation, definitive diagnosis depends upon this measurement The need for and effects of treatment also may be evaluated by this measurement

Since the diffusing capacity is also a measurement of the size of the pulmonary alveolar capillary surface area available for gas exchange severe reduction of this function is probably a contraindication to resectional lung surgery (Chap 9) In addition the degree to which mitral stenosis has produced irreversible pulmonary fibrosis may be reflected in this measurement (Chap 3) Finally the level of the diffusing capacity provides a diagnostic separation between asthma and emphysema (Chap 6)

Limitations

A great many factors affect the diffusing capacity of the lung and may affect the oxygen and carbon monoxide methods differently There are also many technical problems in obtaining an accurate measurement of the diffusing capacity Nevertheless the test has proved to be a valuable clinical tool in the situations mentioned above and as the factors involved in the measurments become clearer and as they become susceptible to separate analysis by refined techniques the study of diffusion may attain even more value

EXERCISE TESTS

Technique

A physician utilizes an exercise test every time he asks a patient to describe the situations in which he experiences shortness of breath the length of time it takes to develop the severity of the work involved and the severity of the symptom In the laboratory exercise tests may involve stepping up and down on a platform walking

RIGHT HEART CATHETERIZATION

BLOOMFIELD R A LAUSON H D COURNAND A BREED E S and RICHARDS D W JR Recording of right heart pressures in normal subjects and in patients with chronic pulmonary disease and various types of cardio circulatory disease *J Clin Invest* 25 639 1946

GORLIN R and GORLIN S G Hydraulic formula for calculation of the area of the stenotic mitral valve other cardiac valves and central circulatory shunts *Am Heart J 41* 1 1951

KORNER, P I and SHILLINGFORD J P Further observations on the estimation of valvular incompetence from indicator dilution curves *Clin Sc 15* 417 1956

MICHEL D HERBST M HARTLEB O and BLOCK K The diagnostic significance of the oxygen step in cardiac catheterization *Ztschr Kreis laufforsch 44* 902 1955

OPDYKE D F Interpretation of cardiovascular pressure pulses *Circulation 17* 481 1958

RICHARDS D W JR Right heart catheterization *Science 125* 1181 1957

SCEBAT L. RENAIS J MEEUS BITHE L and LENÈGRE J Accidents indica tions et contre indications due cathétérisme des cavites droites du cœur *Arch mal cœur 50* 943 1957

SLOAN H MORRIS J D FIGLEY M and LEE R Temporary unilateral occlusion of the pulmonary artery in the preoperative evaluation of thoracic patients *J Thoracic Surg 30* 591 1955

SWAN H J C BURCHELL H B and WOOD E H Special applications of indicator-dilution techniques in congenital and acquired heart disease *Proc Staff Meet Mayo Clin 31* 486 1957

YU P N LOVEJOY F W JOOS H A NYE R E BEATTY D C and SIMPSON J H Pulmonary capillary pressure in various cardiopulmonary diseases at rest and under stress *Am Heart J 49* 31 1955

LEFT HEART CATHETERIZATION

ANKENEY J L FISHMAN A P and FRITTS H W JR An analysis of normal and abnormal left atrial pressure pulse in man *Circulation Res* 4 95 1955

BAGGER M BJORK V O and MALMSTROM G Technique and sequelae of catheterization of the left side of the heart *Am Heart J 53* 91 1957

BRAUNWALD E TANENBAUM J L and MORROW A G Localization of left to right cardiac shunts by dye dilution curves following injection into the left side of the heart and into the aorta *Am J Med 24* 203 1958

CROWLEY W P JR and PARKIN T W Experience with and sequelae of catheterization of the left side of the heart via the percutaneous route *Proc Staff Meet Mayo Clin 31* 115 1956

GOLDBERG H SMITH R. C and RABER G Estimation of severity of aortic stenosis by combined heart catheterization *Am J Med 24* 853 1958

Limitations

Exercise tests must be performed under the careful supervision of a physician and should be carried out after the subject has become accustomed to the apparatus and to the particular type of exercise involved This is not a problem in the case of treadmill exercise, but an untrained subject may have difficulty performing a supine pedal type exercise if he has never done it before Many measurements particularly that of cardiac output by the Fick principle require that the oxygen uptake and cardiac output be stable over the period of time during which samples are collected This requires that the intensity of exercise be kept constant during the test and this is often difficult for weak or dyspneic patients Finally, it is important not to push the patient beyond the capacity of his cardiopulmonary system, particularly an individual with ischemic heart disease and potential myocardial ischemia

An important limitation concerns the application of results obtained during relatively acute exercise in the laboratory to the performance of work during one s daily life Satisfactory performance of a 5 minute exercise test does not necessarily mean that a patient can carry out the same level of work for a longer period of time, and much more information is needed before one can translate the results of such rather short exercise tests to the performance of daily tasks and occupations The problem of prolonged exertion—the factors limiting one s capacity to perform sustained work—requires a great deal more study

REFERENCES

GENERAL

ARNOTT W M Order and disorder in pulmonary function *Brit M J* 2 279 1955

COMROE J H JR Interpretation of commonly used pulmonary function tests *Am J Med* 10 356 1951

COMROE J H JR, FORSTER R E II DUBOIS A B BRISCOE W A and CARLSEN E *The Lung* Chicago Year Book Publications 1955

GORDON B L Ed *Clinical Cardiopulmonary Physiology* New York Grune & Stratton 1957

RUSHMER R F *Cardiac Diagnosis* Philadelphia Saunders 1955

WIGGERS C J *Circulatory Dynamics* Grune & Stratton 1952

ROCHELLE R H Range and variability of measurements of venous pressure in man by direct manometry *J Appl Physiol 10* 523 1957

VENTILATORY STUDIES

FRANKLIN W MICHELSON A L LOWELL F C and SCHILLER I W Clinical value of a tracing of forced expiration (expirogram) 1 Pulmonary disease *New England J Med 253* 799 1955

GAENSLER E A Analysis of the ventilatory defect by timed vital capacity measurements *Am Rev Tuberc 64* 256 1951

LEUALLEN E C and FOWLER W S Maximal midexpiratory flow *Am Rev Tuberc & Pulmonary Diseases 72* 783 1955

MILLER W F JOHNSON R L and WU N The half second expiratory capacity test a convenient means of evaluating the nature and extent of pulmonary ventilatory insufficiency *Dis Chest 30* 33 1956

MOTLEY H L The use of pulmonary function tests for disability appraisal including evaluation standards in chronic pulmonary disease *Dis Chest 24* 378 1953

BRONCHOSPIROMETRY

BIRATH G STALLBERG-STENHAGEN S and SWENSON E W Significance of bronchospirometric values *Am Rev Tuberc & Pulmonary Diseases 75* 699 1957

GAENSLER E A Bronchospirometry 1 Review of the literature *J Lab & Clin Med 39* 917 1952

GAENSLER E A and WATSON T R Bronchospirometry III Complications contraindications technique and interpretations *J Lab & Clin Med 40* 223 1952

MECHANICS OF BREATHING

DAYMAN H Mechanics of airflow in health and in emphysema *J Clin Invest 30* 1175 1951

DUBOIS A B BOTELHO S Y and COMROE J H JR A new method for measuring airway resistance in man using a body plethysmograph values in normal subjects and in patients with respiratory disease *J Clin Invest 35* 327 1956

FENN W O Mechanics of respiration *Am J Med 10* 77 1951

FRY D L EBERT R V STEAD W W and BROWN C C The mechanics of pulmonary ventilation in normal subjects and in patients with emphysema *Am J Med 16* 80 1954

MARSHALL R and DUBOIS A B The measurement of the viscous resistance of the lung tissues in normal man *Clin Sc 15* 161 1956

MCILROY M B and ELDRIDGE F L The measurement of the mechanical properties of the lungs by simplified methods *Clin Sc 15* 329 1956

MORROW A G BRAUNWALD E HALLER J A and SHARP E H Left heart catheterization by the transbronchial route technic and applications in physiologic and diagnostic investigations *Circulation 16* 1033 1957

MOSCOVITA H L *et al* Use of simultaneous left heart pressure pulse measurements in evaluating the effects of mitral valve surgery *Am J Med 18* 406 1955

WOOD E H SUTTERER W SWAN H J C and HELMHOLZ H F The technic and special instrumentation problems associated with catheterization of the left side of the heart *Proc Staff Meet Mayo Clin 31* 108 1956

CARDIAC OUTPUT

ASMUSSEN E and NIELSEN M Cardiac output during muscular work and its regulation *Physiol Rev 35* 778 1955

DOW P *Estimations of cardiac output and central blood volume by dye* dilution *Physiol Rev 36* 77 1956

HAMILTON W F Physiology of the cardiac output *Circulation 8* 527 1953

CIRCULATION TIME

CONN H L JR HEIMAN D F and JOYNER C R Measurement of cardiac output and central volume by a modified decholin test of circulation time *Circulation 15* 245 1957

WEXLER J and WHITTENBERGER J L An objective method for determining circulation time from pulmonary to systemic capillaries by the use of the oximeter *J Clin Invest 25* 447 1946

WILLIAMS M H JR A simple method for measuring the lung to ear circulation time with an ear oximeter *J Appl Physiol 9* 299 1956

ANGIOCARDIOGRAPHY

DOTTER C T and STEINBERG I Angiocardiography in congenital heart disease *Am J Med 12* 219 1952

KJELLBERG S R MANNHEIMER E RUDHE U and JONSSON B *Diagnosis of Congenital Heart Disease* Chicago Year Book Publishers 1955

LINDE L M ADAMS F H and O LAUGHLIN B J Endocardial fibroelastosis angiocardiographic studies *Circulation 17* 40 1958

ARTERIAL AND VENOUS PRESSURE

ALBERT R E and EICHNA L W The response of the peripheral venous pressure to exercise in congestive heart failure *Am Heart J 43* 395 1952

GORLIN R KNOWLES J H and STOREY C F The Valsalva maneuver as a test of cardiac function Pathologic physiology and clinical significance *Am J Med 22* 197 1957

HANCOCK E W and ABLEMAN W H A clinical study of the brachial artery pulse form with special reference to the diagnosis of aortic valvular disease *Circulation 16* 572 1957

take and pulmonary diffusing capacity in normal subjects at rest and during exercise *J Clin Invest 33* 530 1954

FORSTER R E II Exchange of gases between alveolar air and pulmonary capillary blood pulmonary diffusing capacity *Physiol Rev 37* 391 1957

MARKS A CUGELL D W CADIGAN J B and GAENSLER E A Clinical determination of the diffusion capacity of the lungs Comparison of methods in normal subjects and patients with alveolar-capillary block syndrome *Am J Med 22* 51 1957

RILEY R L SHEPARD R H COHN J E CARROLL D G and ARMSTRONG B W Maximal diffusing capacity of the lungs in normal male subjects of different ages *J Appl Physiol 6* 588 1954

EXERCISE TESTS

BARRATT BOYES B G and WOOD E H Hemodynamic response of healthy subjects to exercise in the supine position while breathing O_2 *J Appl Physiol 11* 129 1957

BRUCE R A Evaluation of functional capacity and exercise tolerance of cardiac patients 1 Functional capacity *Mod Concepts Cardiovas Dis 25* 321 1956

HOLMGREN A Circulatory changes during muscular work in man *Scandinav J Clin & Lab Invest 8* suppl 24 1 1956

MITCHELL J H SPROULE B J and CHAPMAN C B The physiological meaning of the maximal oxygen intake test *J Clin Invest 37* 538 1958

WYNDHAM C H and WARD J S An assessment of the exercise capacity of cardiac patients *Circulation 16* 384 1957

LUNG VOLUMES AND MIXING

Bateman J B Studies of lung capacities and intrapulmonary mixing normal lung capacities *J Appl Physiol 3* 133 1950

Bateman J B Studies of lung volume and intrapulmonary mixing Nitrogen clearance curves apparent respiratory dead space and its significance *J Appl Physiol 3* 143 1950

Bedell G N Marshall R DuBois A B and Comroe J H Jr Plethysmographic determination of the volume of gas trapped in the lungs *J Clin Invest 35* 664 1956

Blair E and Hickam J B Quantitative study of intrapulmonary gas mixing in emphysema *Am J Med 18* 519 1955

Curtis J K Emanuel D and Rasmussen H K Improved apparatus for determining the functional residual capacity of the lung by the open circuit method *Am J Med 18* 531 1955

DeJours P and Rahn H Residual volume measurements by the gas expansion method and nitrogen dilution method *J Appl Physiol 5* 8 1953

Fowler W S Lung function studies III Uneven pulmonary ventilation in normal subjects and in patients with pulmonary disease *J Appl Physiol 2* 283 1949

Fowler W S Intrapulmonary distribution of inspired gas *Physiol Rev 32* 1 1952

Luft U C Roorbach E H and MacQuigg R E Pulmonary nitrogen clearance as a criterion of ventilatory efficiency *Am Rev Tuberc & Pulmonary Diseases 72* 465 1955

Needham C D Rogan M C and McDonald I Normal standards for lung volumes intrapulmonary gas mixing and maximum breathing capacity *Thorax 9* 313 1954

West J B Fowler K T Hugh Jones P and O Donnell T V The measurement of the inequality of ventilation and of perfusion in the lung by the analysis of single expirates *Clin Sc 16* 549 1957

ARTERIAL BLOOD GASES

Campbell E J M and Howell J B I Simple rapid methods of estimating arterial and mixed venous P_{CO_2} *Brit M J 1* 458 1960

Donald K W Renzetti A Riley R L and Cournand A Analysis of factors affecting concentrations of oxygen and carbon dioxide in gas and blood of lungs Results *J Appl Physiol 4* 497 1952

Lundsgaard C and Van Slyke D D Cyanosis *Medicine 2* 1 1923

Williams M H Jr Quantitative relationships between hypoxemia and disorder of pulmonary function *Yale J Biol & Med 30* 306 1958

DIFFUSING CAPACITY

Bates D V The measurement of the pulmonary diffusing capacity in the presence of lung disease *J Clin Invest 37* 591 1958

Filley G F MacIntosh D J and Wright G W Carbon monoxide up

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